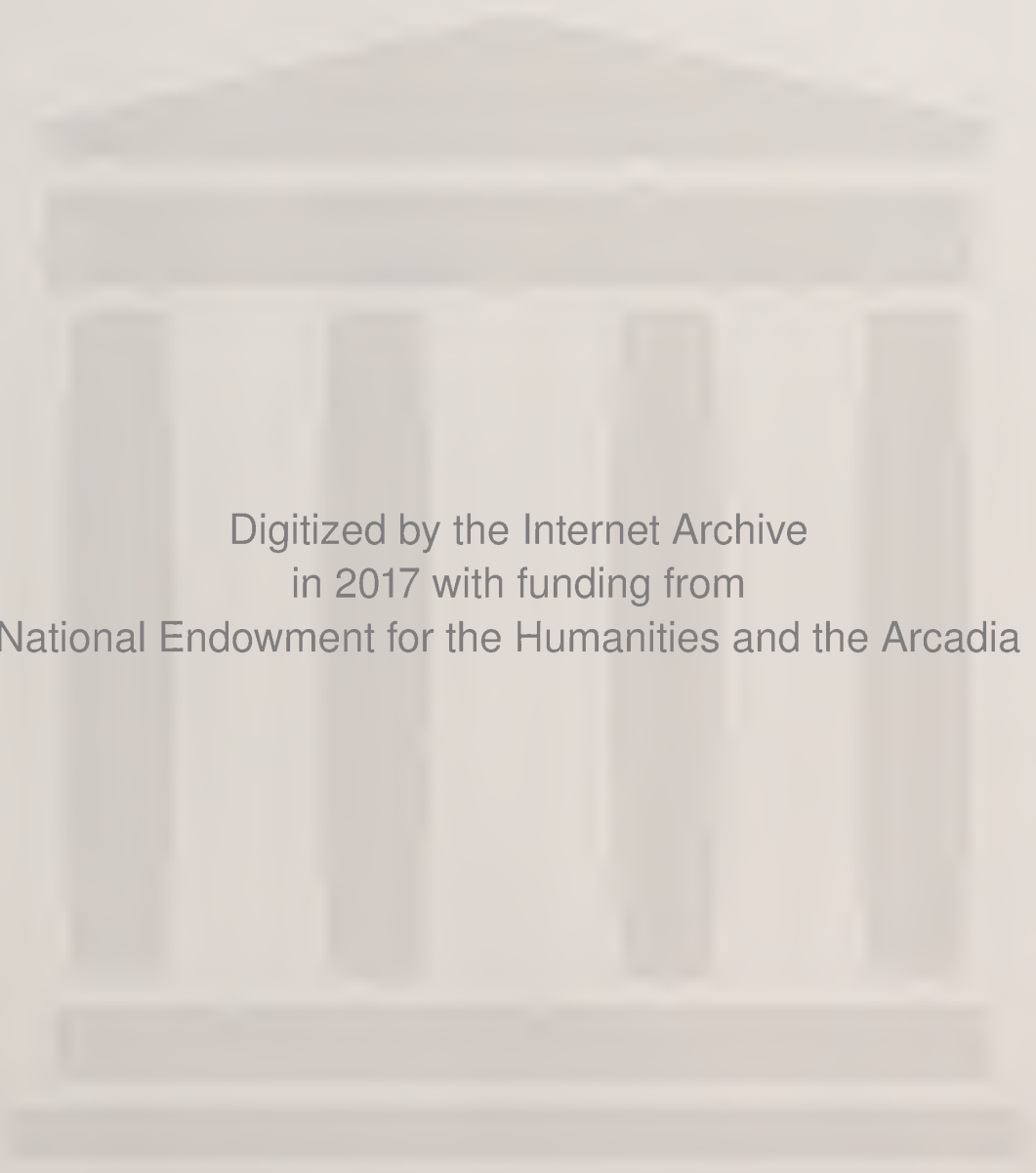


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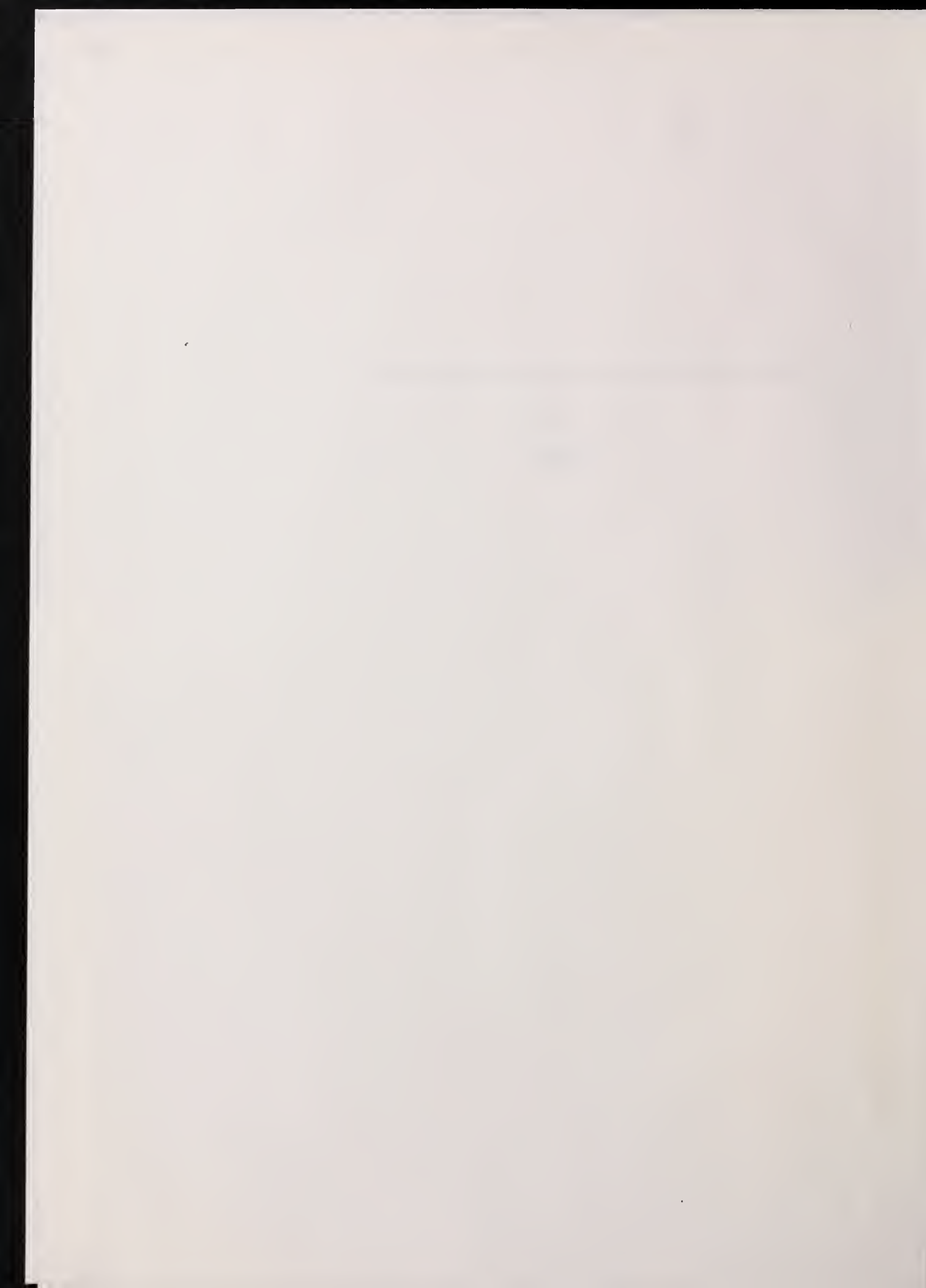


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Boletin Asociacion Medica De Puerto Rico

Vol 72 No 1

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BOLETIN

ASOCIACION MEDICA DE PUERTORICO

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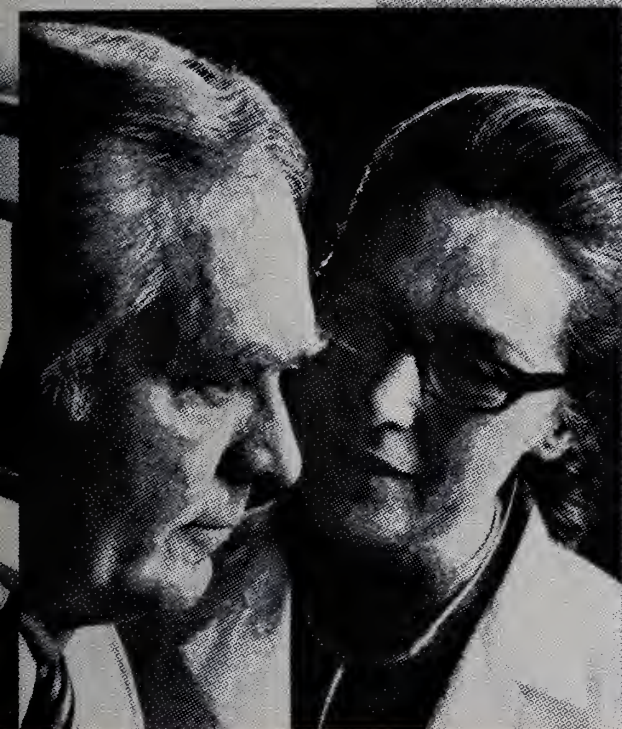
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Contraindications: Patients with known hypersensitivity to the drug

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Usage in Pregnancy: Use of minor tranquilizers during first trimester should almost always be avoided because of increased risk of congenital malformations as suggested in several studies. Consider possibility of pregnancy when instituting therapy; advise patients to discuss therapy if they intend to or do become pregnant.

Precautions: In the elderly and debilitated, and in children over six, limit to smallest effective dosage (initially 10 mg or less per day) to preclude ataxia or oversedation, increasing gradually as needed and tolerated. Not recommended in children under six. Though generally not recommended, if combination therapy with other psychotropics seems indicated, carefully consider individual pharmacologic effects, particularly in use of potentiating drugs such as MAO inhibitors and phenothiazines. Observe usual precautions in presence of impaired renal or hepatic function. Paradoxical reactions (e.g., excitement, stimulation and acute rage) have been reported in psychiatric patients and hyperactive aggressive children. Employ usual precautions in treatment of anxiety states with evidence of impending depression, suicidal tendencies may be present and protective measures necessary. Variable effects on blood coagulation have been reported very rarely in patients receiving the drug and oral anticoagulants: causal relationship has not been established clinically.

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tablets & elixir



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moderate to severe pain

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Description

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Elixir: Each 5 ml. contains 12 mg codeine phosphate[®] plus 120 mg acetaminophen (alcohol 7%)

***Warning:** May be habit forming

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Contraindications: Hypersensitivity to acetaminophen or codeine

Warnings: Drug dependence. Codeine can produce drug dependence of the morphine type and may be abused. Dependence and tolerance may develop upon repeated administration. prescribe and administer with same caution appropriate to other oral narcotics. Subject to the Federal Controlled Substances Act.

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Usage in pregnancy: Safe use not established. Should not be used in pregnant women unless potential benefits outweigh possible hazards.

Pediatric use: Safe dosage of this combination has not been established in children below the age of three.

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Special risk patients: Administer with caution to certain patients such as the elderly or debilitated and those with severe impairment of hepatic or renal function, hypothyroidism, Addison's disease, and prostatic hypertrophy or urethral stricture.

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Drug Interactions: CNS depressant effect may be additive with that of other CNS depressants. See Warnings. For information on symptoms/treatment of overdosage, see full prescribing information.

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TYLENOL with Codeine tablets are manufactured by McNeil Laboratories Co., Dorado, Puerto Rico 00646.

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Elixir Each 5 ml contains 12 mg codeine phosphate* plus 120 mg acetaminophen (Alcohol 7%)

*Warning: May be habit forming.

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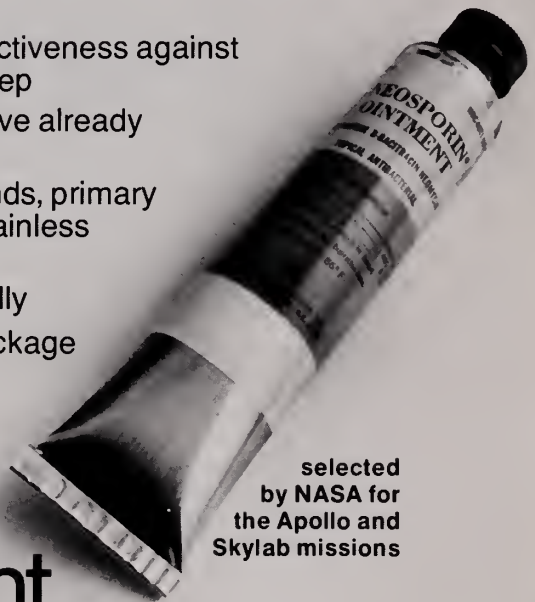
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WARNING: Because of the potential hazard of nephrotoxicity and ototoxicity due to neomycin, care should be exercised when using this product in treating extensive burns, trophic ulceration and other extensive conditions where absorption of neomycin is possible. In burns where more than 20 percent of the body surface is affected, especially if the patient has impaired renal function or is receiving other aminoglycoside antibiotics concurrently, not more than one application a day is recommended.

When using neomycin-containing products to control secondary infection in the chronic dermatoses, it should be borne in mind that the skin is more liable to become sensitized to many substances, including neomycin. The manifestation of sensitization to neomycin is usually a low grade reddening with swelling, dry scaling and itching; it may be manifest simply as a failure to heal. During long-term use of neomycin-containing products, periodic examination for such signs is advisable and the patient should be told to discontinue the product if they are observed. These symptoms regress quickly on withdrawing the medication. Neomycin-containing applications should be avoided for that patient thereafter.

PRECAUTIONS: As with other antibacterial preparations,

prolonged use may result in overgrowth of nonsusceptible organisms, including fungi. Appropriate measures should be taken if this occurs.

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Complete literature available on request from Professional Services Dept. PML.



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ASOCIACION MEDICA DE PUERTORICO

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NOTA DEL EDITOR

La Asociación Médica de Puerto Rico y la Junta Editora se complacen en presentar en esta edición el simposio sobre Trasplantes Renales celebrado en la pasada sesión científica de la Asociación Médica de Puerto Rico.

Los doctores Santiago Delpín y Ramírez González han colaborado en la preparación de esta edición repasando los trabajos y editando manuscritos de tal manera de presentar en forma concisa y exacta el problema de la enfermedad renal y los resultados de trasplantes en Puerto Rico.

Los resultados tal y como se presentan en esta edición son excelentes. El 66 por ciento de los pacientes tienen una rehabilitación total a largo plazo y la función renal en la mayoría de los pacientes operados es prácticamente normal.

Después de analizar los trabajos presentados y reflexionar sobre las conclusiones de los autores es aparente que el mayor logro del programa de trasplantes en Puerto Rico fue el de combinar los esfuerzos y habilidades de un gran número de profesionales médicos y paramédicos procedentes de diferentes instituciones del país. Este esfuerzo combinado es ingrediente indispensable para lograr el éxito en una empresa de esta magnitud.

Exhorto a todos nuestros lectores a leer los resultados del programa de trasplante renal, pero más importante, a reflexionar sobre lo que se podría lograr a través de la coordinación de esfuerzos y facilidades existentes en nuestras instituciones y centros docentes.

Juan M. Aranda, MD, FACC

LOS TRASPLANTES EN PUERTO RICO

Hace ya más de 25 años que se comenzó la actividad de trasplantes en Europa y América, 12 años de los esfuerzos iniciales en nuestro país, y 3 años desde que comenzó el Programa de Trasplantes de Puerto Rico. Aunque la sustitución de órganos está en este momento en la vanguardia de la investigación médica mundial, los prestadores de servicios médicos, los filósofos de la medicina, y los sociólogos, todos concuerdan en que se refleja tan solo una etapa temporera en la evolución de la terapéutica. Y aunque de un impacto dramático, mudo reflejo es el tener que trasplantar, del poco conocimiento que tenemos todavía sobre la causa de las enfermedades. La intervención en el futuro estará dirigida a la prevención y el manejo temprano de las enfermedades que destruyen los órganos que hoy sustituimos. Pero antes de que lleguemos a tan ideal realidad, veremos muchos más trasplantes de órganos y de tejidos. Trasplantaremos tejidos de potencial inmunológico. Trasplantaremos tejidos en sustitución de hormonas y encimas. Trasplantaremos membranas, receptores, la cubierta de nuestro cuerpo. Eventualmente, trasplantaremos para sustituir las moléculas reguladoras de las diferentes funciones biológicas.

Pero uno de los beneficios más significativos que se ha visto con los trasplantes, y quizás la contribución más profunda a la ciencia moderna, lo ha sido el precipitar, forzar, imponer una investigación intensa en el campo de la inmunología. Conjuntamente con los inmunólogos de cáncer, los inmunólogos de trasplante en su búsqueda de cómo doblegar sin abrogar la respuesta inmune, han avanzado el conocimiento de éste tan central sistema biológico.

Contribución de igual magnitud ha sido el enfocar al paciente como persona: el traer al foro legal y sociológico mundial problemas de gran significado para nuestro futuro; el apurarse por reestablecer al hombre como contribuyente, como aportador, con obligación hacia su familia y sociedad, y a la vez con derecho al disfrute de una vida plena y no de una vida trunca y dependiente, aunque fuera ésta más larga.

Testigo elocuente de la variedad de enfoques y de estudiosos envueltos en el campo del trasplante lo es esta edición del Boletín. La gama de investigación clínica, básica, sociológica, psicológica aquí descrita refleja también la unión y síntesis de disciplinas y personas que tradicionalmente estaban aisladas entre sí. Insinúa la cohesión del conocimiento humano. Ilustra la aportación tan significativa e imprescindible de todas las personas envueltas en la prestación de este servicio. Ilustra además, que nuestro principal recurso es el propio ser humano.

Eduardo A. Santiago Delpín, MD
Rafael Ramírez González, MD

EL PROBLEMA DE LA ENFERMEDAD RENAL EN PUERTO RICO Y SU TRATAMIENTO CON DIALISIS Y TRASPLANTE

Rafael E. Ramírez-González, MD

El paciente con enfermedad renal permanente en Puerto Rico tiene las siguientes alternativas de tratamiento a su disposición:

A) *Diálisis*

1) Hemodiálisis

- a) intra-hospitalaria
- b) satélite
- c) en el hogar

2) Diálisis Peritoneal

- a) intermitente
- b) ambulatoria-continua (CAPD)

B) *Trasplante Renal*

- 1) Donante vivo, relacionado
- 2) Cadáver

El costo de estas modalidades de tratamiento es alto y varía desde \$8,000 anuales para hemodiálisis en el hogar hasta \$25,000

anuales para un trasplante exitoso. Por esta razón, el gobierno federal ha reconocido la enfermedad renal permanente como una enfermedad catastrófica y aprobó legislación (PL-95-292) para cubrir casi en su totalidad, los costos de este tipo de tratamiento.

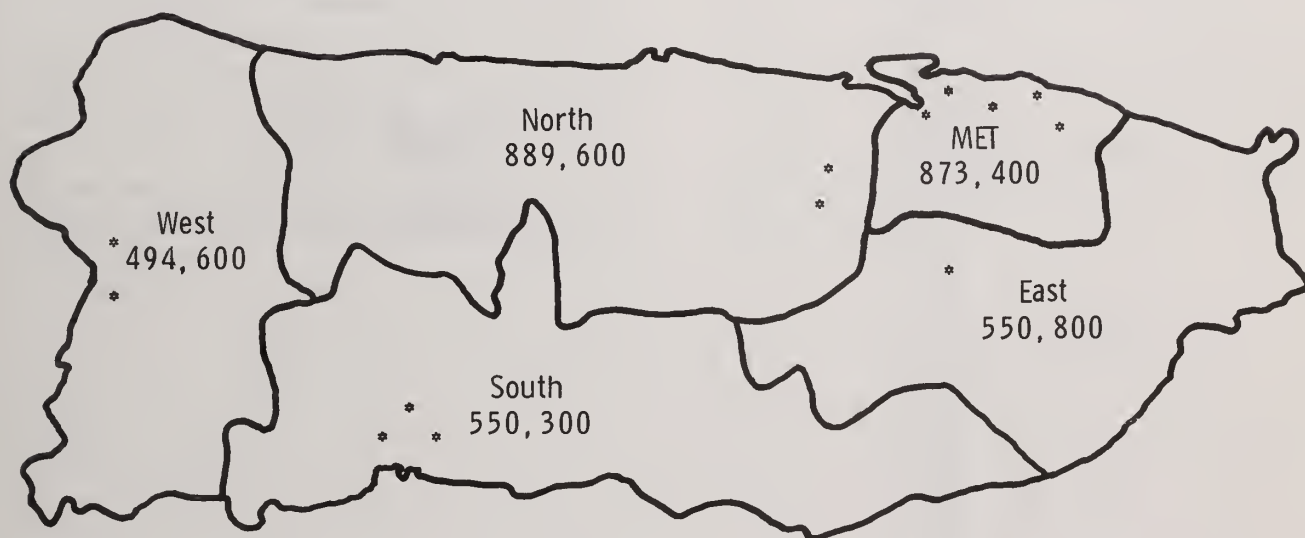
Para implementar la ley y hacer llegar a cada paciente el tratamiento que necesita, se crea una red de Consejos Coordinadores a través de la nación. En Puerto Rico, el Consejo Coordinador de Enfermedades Renales Permanentes Núm. 29, coordina la implementación de la ley PL-95-292 en Puerto Rico y las Islas Vírgenes.

El Consejo Coordinador en Puerto Rico está compuesto por representantes de las siguientes disciplinas de la salud:

- 1) Nefrólogos
- 2) Nefrólogos pediátricos
- 3) Internistas
- 4) Cirujano de Trasplante
- 5) Enfermera de diálisis
- 6) Tecnólogo de diálisis
- 7) Dietista renal
- 8) Trabajadora social renal
- 9) Administradores de facilidades de tratamiento dialítico

ESRD HEALTH REGIONS AND FACILITIES
ESTIMATED POPULATION 1978

Figure #1



Source of Information: Statistical Report -
to ESRD Patient - 1978 Report NCC #29

- 10) Representantes de los pacientes renales
- 11) Representante del laboratorio de Histocompatibilidad
- 12) Representantes de cada facilidad de tratamiento

Esta representación garantiza que en la planificación de los servicios renales no se omita ningún aspecto importante del cuidado integral del paciente renal.

La incidencia de enfermedad renal permanente en Puerto Rico es de 92 *pacientes nuevos*/1,000,000 de habitantes por año. Pa-

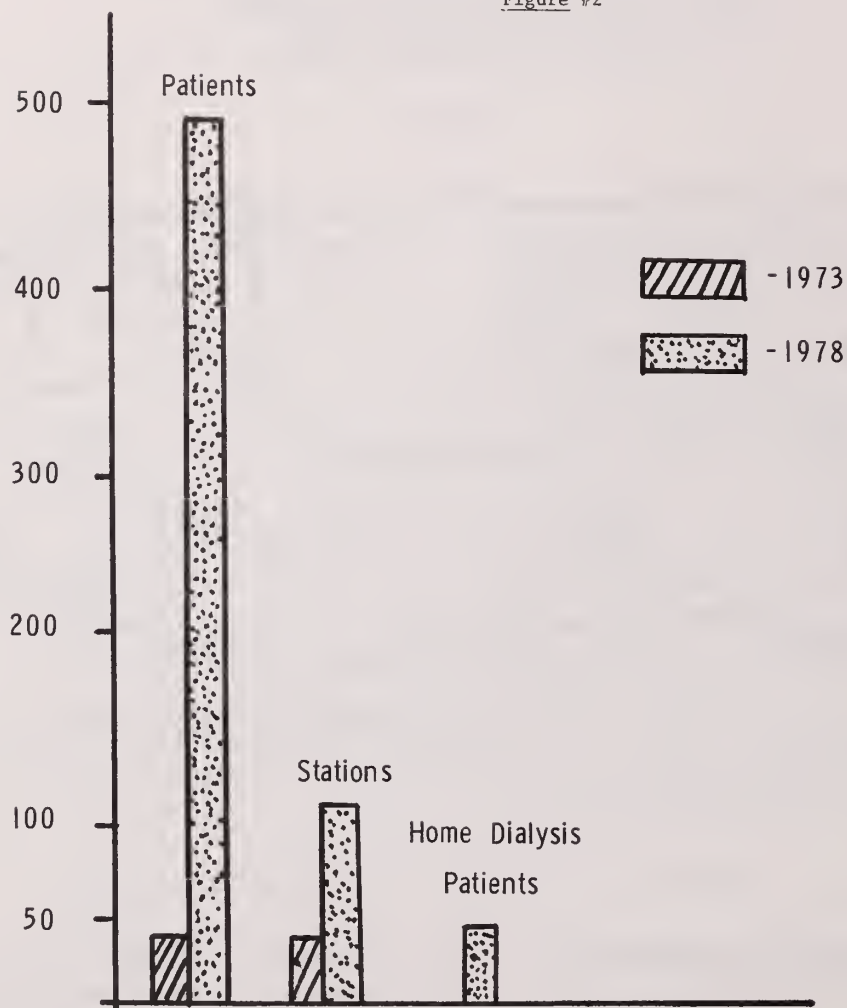
ra la población de nuestra isla esto representa un total de aproximadamente 294 *pacientes nuevos por año*. Esta cifra se obtuvo de las estadísticas del consejo coordinador para 1978.

Para servir a esta población de pacientes renales, nuestra isla cuenta con 12 facilidades de tratamiento dialítico distribuidas entre 5 regiones de salud. (Ver Fig. 1). Estas son las siguientes:

- 1) Auxilio Mutuo
- 2) BMA San Juan
- 3) San Juan City Hospital

ESRD PATIENTS AND SERVICES

Figure #2



Source of Information: Statistical Report -
to ESRD Patient - 1978 Report NCC #29

- 4) University District Hospital
- 5) Veterans Administration Hospital
- 6) BMA Mayaguez
- 7) Mayaguez Medical Center
- 8) BMA Ponce

- 9) Ponce District Hospital
- 10) Santo Asilo de Damas
- 11) Centro Nefrológico del Caribe, Bayamón
- 12) Hospital San Pablo, Bayamón

Está en vías de aprobarse la facilidad de la re-

gión Este, pero al momento todavía no está en operaciones.

La relación de pacientes renales y facilidades de tratamiento dialítico puede verse en la figura 2. Esta figura compara lo que teníamos en 1973 con lo que contamos en 1978.

El programa de trasplante renal de Puerto Rico está físicamente localizada en el Hospital de Veteranos. Hasta la fecha se han llevado a cabo 47 operaciones de trasplante de riñón con resultados comparables a los mejores centros en E. U. Los detalles de este programa aparecen discutidos en otros trabajos en este simposio.

En resumen, podemos concluir que nuestra isla cuenta con 12 facilidades de tratamiento dialítico distribuidas entre las cinco regiones de salud. La región Este será servida por una facilidad adicional que está en planes de abrirse en el Hospital Sub-Regional de Caguas. Contamos con un programa de trasplante renal activo y exitoso. Al día de hoy mantenemos alrededor de 600 pacientes en diálisis crónica y hemos trasplantado 47 pacientes. Esta actividad es coordinada a través del Consejo Coordinador de Enfermedades Renales de P. R. e Islas Vírgenes.

TECHNICAL ASPECTS OF RENAL TRANSPLANTATION SURGERY OF THE RECIPIENT AND UROLOGIC COMPLICATIONS

Andrés Acosta Otero, MD and Roberto Fortuño, MD

Excellent and detailed reviews and illustrations of renal transplantation have been published recently. (1-4) This brief account is based on those works and on experience with our Transplant Program. We shall review the main surgical details of the renal transplant adult recipient's operation, and discuss the more frequent urologic complications. Donor surgery, vascular and medical complications, as well as the statistics of our series, are discussed elsewhere in this Symposium.

Technique

In adults, the kidney is implanted in the iliac region because of the relatively easy access to excellent blood supply from the iliac vessels. This location also offers some protection from external trauma, and permits extraperitoneal placement of the organ, thereby avoiding gastrointestinal complications after initial and sometimes repeated surgical approaches. The recipient usually undergoes hemodialysis the day before surgery. Time is allowed for disappearance of the effects of the heparin used during the hemodialysis.

After the recipient is fully anesthetized, and the vascular access for dialysis has been

protected, a Foley catheter of a size adequate for blood clot irrigation (24 F) is inserted under extra-strict aseptic condition; cultures are taken, and the bladder is irrigated and partially filled with a known volume of neomycin solution.

The approach used in most of our adult recipients is an abdominal oblique lower quadrant incision which usually extends from a point anterior and superior to the iliac crest to a point above the symphysis pubis, near the midline. The external oblique aponeurosis is incised along its fibers, its superior flap separated bluntly from the internal oblique, and the rectus sheath is incised longitudinally. The rectus muscle is retracted medially and the posterior rectus sheath is incised, thereby entering the retroperitoneal space and space of Retzius. The inferior epigastric vessels are usually ligated and divided near the inguinal ligament, but we try to dissect and retract the spermatic cord, to avoid having to divide it. There is less devitalization of muscle with this approach than with previous techniques involving transection of the internal oblique muscle. (As urologists we find it a vital addition to our resources in dealing with the notorious lower ureter).

During dissection of the iliac vessels and when space is being developed retroperitoneally for the graft, fastidious hemostasis and lymphostasis are practiced to avoid fluid accumulations, particularly lymphocele. Careful ligation and division of posterior affluents of the external iliac vein allow its mobilization

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for ease of venous anastomosis. This is particularly true when dealing with the frequently short right renal vein. Since a termino-terminal arterial anastomosis has proven superior, the internal iliac artery is divided and occluded atraumatically, until the time of anastomosis to the renal artery. A convenient segment of the freed external iliac vein is temporarily occluded at both ends, and an ellipse is removed from the anterolateral aspect of the vein.

If a live donor is used, vascular occlusion for removal of the organ from the donor (prior to cold perfusion) is timed for least duration of ischemia by communication with the recipient team. If the kidney has been removed from a cadaver, it is brought from the preservation module, already cooled and perfused, ready for implantation. The vein is anastomosed first, using a running suture of fine synthetic polymer. The renal vein is then clamped, to avoid retrograde perfusion of the kidney, and the iliac vein clamps are removed, restoring venous drainage from the leg. The arterial anastomosis is performed with fine synthetic polymer. The arterial intima must be handled carefully when perfusing with a cannula, as well as when dilating the vessel prior to anastomosis.

When the arterial anastomosis is complete, the vascular clamps are removed and (in majority of cases) immediate urination through the graft ureter is observed. The graft ureter is implanted in the bladder in an approximately 3 cm. submucosal tunnel, distal to its entrance histus in the bladder. Bladder closure is accomplished in layers, using absorbable suture for the mucosa and nonabsorbable synthetic material for the external layers. The Foley catheter is usually removed in twenty-four hours. No stents or drains are used, since these might contribute to infection, and one cannot afford such a risk in a patient who will receive immunosuppression.

Urologic Complications

Over the past few years both patient survival and graft survival have improved; however, improvement has been greater in patient survival. In addition to a better preparation with hemodialysis and more judicious immunosuppression, a significant factor has been an improved awareness of when to cease trying to save the graft, in order to preserve the patient's life.

Urologic complications frequently contribute to graft loss and patient's death. Mortality from urologic complications have been reported as high as 68 percent in some series; morbidity from 4 to 30 percent. The most common urologic complications are urine leaks and ureteral obstruction. Impotence after a second transplant has been reported too.

(1) *URINE LEAKS*: Extravasation may occur from the ureter or from the bladder.

(a) *Uretero-cutaneous fistula* (with a 3 to 10 percent incidence) is usually the result of vascular insufficiency from damage to the ureteral blood supply during donor nephrectomy. It is more common in live donor series, because more dissection of the vessels is needed than in the cadaver, where "en bloc" excision is usually performed. Diabetics also have a higher risk of ureteral leak. Diagnosis is usually made by urography or cystography. The high mortality associated with this condition makes prompt management mandatory. Anastomosis of donor pelvis to recipient ureter is the corrective procedure of choice, but if this is not possible, pyelo-vesicostomy by bladder mobilization is advised.

(b) *Vesical fistulas* are usually due

to poor closure technique and/or obstruction of the catheter by blood clots, etc. Management, depending on severity, varies from temporary catheter drainage to surgical closure.

(c) *Calyceal fistula* may occur when polar vessels of the graft are sacrificed and regional renal infarction results in necrosis and leakage.

(2) *OBSTRUCTION* occurs in 1.1 to 10.7 percent of the cases, and is most commonly due to technical error during ureteral implantation, such as implantation of the mobile portion of the bladder, tension, torsion, misplaced sutures or angulation. Late obstruction may result from fibrosis or fibrotic bands. Management depends on the cause and ranges from temporary intubation for edema, to reimplantation, or use of the recipient's ureter as a substitute. Extrinsic compression by the spermatic cord is avoided by placement of the ureter deep to the spermatic cord. (When the spermatic cord has to be divided, the incidence of ipsilateral hydrocele is high).

(3) *IMPOTENCE*: This serious complication, which adds to the already increased rate of impotence among chronic dialysis patients, has been reported in cases where a second transplant is needed and the remaining internal iliac artery is divided. Several authors have proposed the remedy: end-to-side arterial anastomosis of the graft artery to the external

iliac artery of the recipient.

Urinary Diversion

On occasion the bladder may be scarred, infected, damaged, or otherwise diseased so as to render it non-functional. We have had three such cases in children. To correct this problem a preliminary operation was performed in each before transplantation. In one 10 year-old boy an iliocecal conduit was constructed. In an 8 year-old girl an ilial loop was done, and in a 14 year-old boy a previously-constructed, mature, well-functioning cutaneous ureterostomy was used. Subsequently, the transplanted ureter was anastomosed to the artificial conduit. All three patients have fared well from the urologic point of view, with the exception of a revision done on the iliocecal conduit because of prolapse of mucosa.

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EL DONANTE DE RIÑÓN

Ernesto Rive Mora, MD, FACS and José H. Amadeo, MD, FACS

En la actualidad solo existen dos formas de obtener riñones para trasplantar a pacientes con enfermedad renal terminal que cualifiquen para trasplante:

1. Donante vivo familiar cercano del recipiente.
2. Cadaver - no relacionado con el recipiente.

Donante Vivo

El riñón en mejores condiciones y con mayor probabilidad de compatibilidad y éxito de trasplante se obtiene de esta forma. Esto obedece a que así se puede escoger el riñón más histocompatible con el recipiente y por tanto se reduce la incidencia de rechazo irreversible. También se reduce el período de anoxia que sufre el riñón a un mínimo, consiguiéndose así un riñón en mejores condiciones. Solo usamos donantes que sean parientes cercanos y en perfecto estado de salud.

Los criterios establecidos para cualificar como donante son los siguientes:

Edad: 21-59 años de edad, en algunas situaciones especiales se extiende la edad de 18 - 65 años. En donantes menores de edad es necesario obtener

permiso legal a través de la corte.

Estado perfecto de salud.

Riñones y tractos urinarios normales.

Relación familiar - El orden de preferencia es el siguiente:

Hermano gemelo idéntico.

Hermano no gemelo pero genéticamente igual (A-Match).

Hermanos no gemelos.

Padres o hijos.

Otra relación familiar cercana.

No se usa donante vivo no familiar.

El proceso a seguir para obtener donantes vivos es:

(Fig. 1) - El recipiente recluta entre sus familiares más cercanos los voluntarios que estén dispuestos a hacer la donación. Este grupo pasa a la fase primera de estudio, la cual no requiere hospitalización. Esta fase preliminar incluye grupo sanguíneo, historia médica y pruebas de histocompatibilidad. Los que cualifican pasan a la segunda fase del estudio. En esta el candidato a donante se hospitaliza y se estudia de la si-

Del Departamento de Cirugía, Administración de Veteranos, San Juan, Puerto Rico.

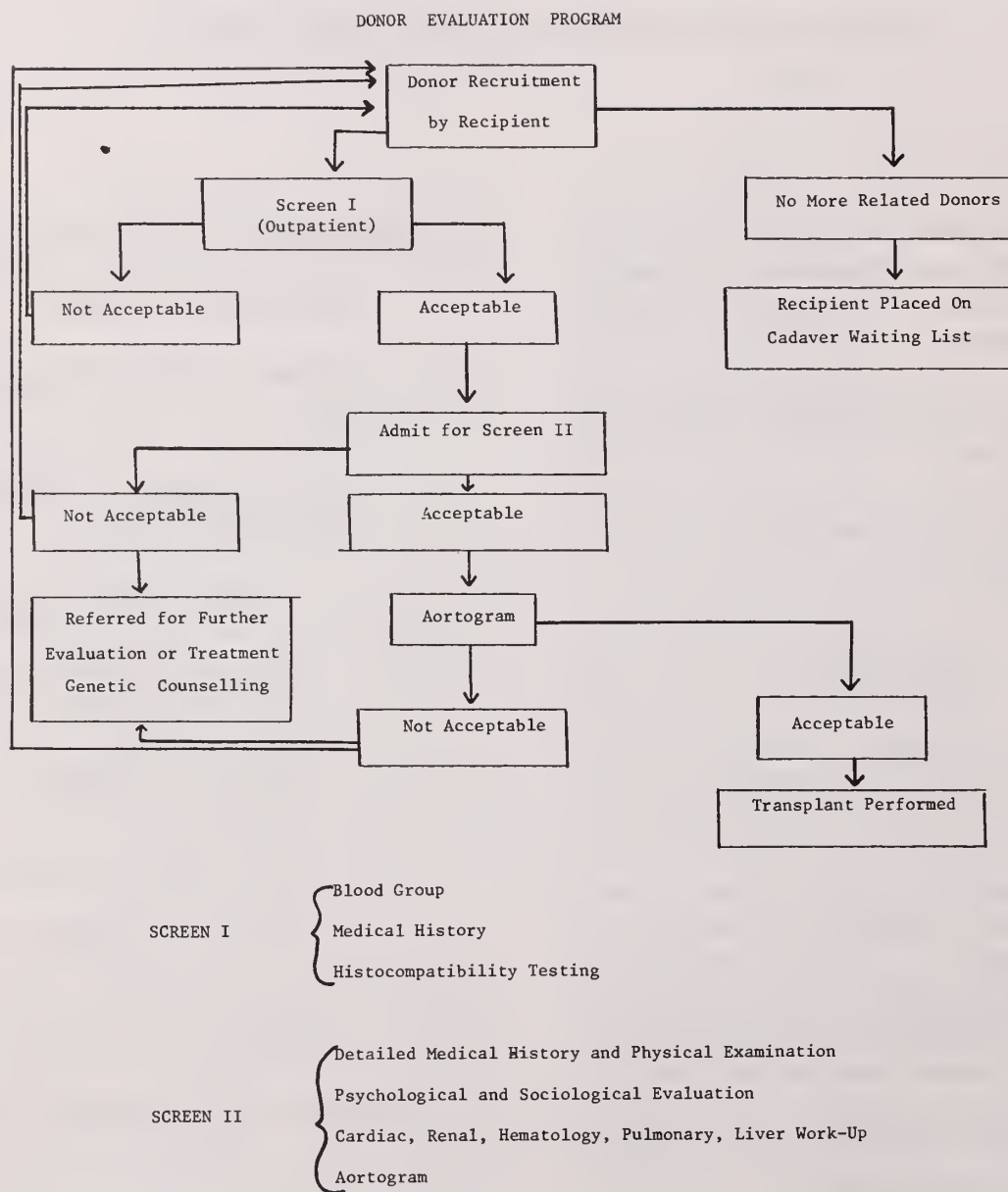


FIGURE 1

guiente manera:

- Historial médico y examen físico detallado.
- Evaluación psicológica y sociológica - debemos estar comple-

tamente seguros de la capacidad y estabilidad mental de estas personas. Queremos asegurar que la decisión de ser donante es hecha libre de presiones ajenas a su voluntad, y también

que la intención y motivación es traída a un nivel conciente y que esta es aceptada tanto por el donante como por el paciente. No queremos problemas futuros, tales como sentido de posesividad o de eterno agradecimiento - "el paciente recibió algo de mí, ahora me pertenece o me debe la vida" - ambivalencia - "te quiero tanto que te di parte de mi cuerpo - te odio por haberme hecho pasar por el trauma de una operación" - resentimiento con el resto de la familia por haberle presionado a donar, y otros.

c. Evaluación completa de sus sistemas:

Cardíaco: electrocardiograma, y otras pruebas adicionales de estar indicadas.

Hepático: batería completa de pruebas sanguíneas hepáticas.

Hematológica: conteo de glóbulos rojos, blancos y diferencial, y plaquetas.

Renal: examen de orina, incluyendo cultivo, pielografía intravenosa y depuración de creatinina en 24 horas.

Pulmonar: Placa de pecho. De estar indicado se obtienen pruebas de función pulmonar.

Si luego de estos estudios el candidato a donante aún cualifica entonces y sólo entonces

se procede a hacerle un aortograma. La aortografía nos demuestra la presencia de cualquier patología o anomalía vascular en los riñones y nos indica cuantos vasos sanguíneos hay en cada lado. Preferimos usar el riñón izquierdo porque la vena renal izquierda es más larga, pero a la misma vez queremos si posible un riñón con una sola arteria pues esto reduce el número de anastomosis vasculares necesarias al ser trasplantado y por lo tanto disminuye el riesgo de errores técnicos y posible pérdida del riñón. Si el aortograma es aceptable y todavía el candidato quiere donar, se le acepta como donante de riñón. En cualquier momento que el posible donante desista de la idea - ahí mismo cesa de ser candidato. En estos casos la explicación que se le da al recipiente es que el donante no cualifica médicamente como tal y por lo tanto ha sido rechazado por nosotros. Nunca se le dice al paciente ni a su familia que un posible donante cambió de parecer - no importa la razón.

Si en alguna de las fases de estudio del candidato a donar se encuentra que este no cualifica médicamente, se rechaza y se refiere para más estudios y/o tratamiento de la condición encontrada. Al recipiente se le notifica que tiene que reclutar otro familiar que esté dispuesto a donar. Si el recipiente no tiene otro candidato a donante - este pasa a la lista de espera de riñón de cadáver - de esto hablaremos más adelante.

Estos estudios tan minuciosos se llevan a cabo para reducir a un mínimo el riesgo en estos donantes que por definición están en perfecto estado de salud y que se van a someter a una operación electiva de magnitud en la cual tienen poco que ganar y mucho que perder. El recipiente por el contrario debido a su enfermedad tiene todas las de ganar y muy poco que perder.

Para mayor objetividad en la selección

o rechazo de un donante, el médico a cargo de este no es el mismo ni tiene nada que ver con el paciente. De hecho el donante y recipiente se hospitalizan en distintos pisos del hospital.

Al donante no debe sucederle ninguna complicación que sea prevenible y es labor del médico a cargo velar por la seguridad tanto física como mental del mismo. Todo lo que le pase a este ser humano bueno o malo es el resultado directo de la decisión médica de aceptarlo y someterlo a la operación.

Como pueden ver la responsabilidad que recae en el médico es mucha. De igual forma la ansiedad, temor al dolor, a lo desconocido, que se genera en el donante es también mucha. Todo esto se acepta porque se prefiere usar donante vivo. La razón la reflejan las estadísticas nacionales de supervivencia a cinco años de un riñón de donante vivo vs. de cadáver: 80 por ciento en el primero y 50 por ciento en el segundo.

Los riesgos a que se somete el donante son en realidad, mínimos. Esto se debe a todo lo antes mencionado. El riesgo operatorio en sí conlleva hasta el presente una mortalidad de cero y complicaciones en un bajo por ciento y todas menores.

La esperanza de vida del nefrectomizado unilateral es igual a la del no operado.

Complicaciones futuras post operatorias - ninguna.

Incapacidad a largo plazo:

Trabajo: puede volver a su trabajo usual en 6 semanas aproximadamente sin ninguna limitación física. No altera ni limita en lo más mínimo su fertilidad ni vida sexual. No lo convierte en un riesgo mayor desde el punto de vista de las compañías aseguradoras de vida.

Inconveniencias producidas por la opera-

ción:

Período usual de hospitalización de 6 a 7 días.

Período postoperatorio en el hospital - 5 días - convalecencia en su hogar 4 a 6 semanas.

La única limitación que se le impone al donante es evitar los deportes de contacto, los cuales se prohíben por razones obvias.

Acto Quirúrgico

La nefrectomía del donante se lleva a cabo simultáneamente con la del recipiente en salas contiguas. El paciente se posiciona en decúbito lateral flexionado a un máximo. En todo momento se sigue el paciente con medidas de producción de orina, presión venosa central, y demás signos vitales. El cirujano del donante tiene la libertad de detener o cancelar la operación en cualquier momento que éste o el anesthesiólogo crea que existe algún riesgo para el paciente. Esta decisión es sola de médico del donante y no se pide parecer, solo se le notifica al personal de la sala del recipiente.

La incisión es antero-lateral en el flanco por debajo del reborde costal. Muchas veces para facilitar la disección y de tal forma proteger el riñón se remueve la costilla número 12 y a veces la parte distal de la costilla número 11. La técnica quirúrgica tiene que ser extremadamente cuidadosa y minuciosa para poder brindar un riñón perfecto con el menor trauma posible. Una vez removido el riñón - su úreter y su pedículo vascular ambos cortados lo más largo posible - se le entrega en las manos al cirujano de trasplante que ha

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El artículo, si se aceptara, será con la condición de que se publicará únicamente en esta revista.

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El manuscrito debe comenzar con una breve introducción en la cual se especifique el propósito del mismo. Las secciones principales (como por ejemplo: materiales y métodos) deben identificarse como un encabezamiento al centro y en letras mayúsculas.

Artículos referentes a resultados de estudios clínicos o investigaciones de laboratorio deben organizarse bajo los siguientes encabezamientos: *Introducción, Materiales y Métodos, Resultados, Discusión, Resumen (en español e inglés), Reconocimiento y Referencias.*

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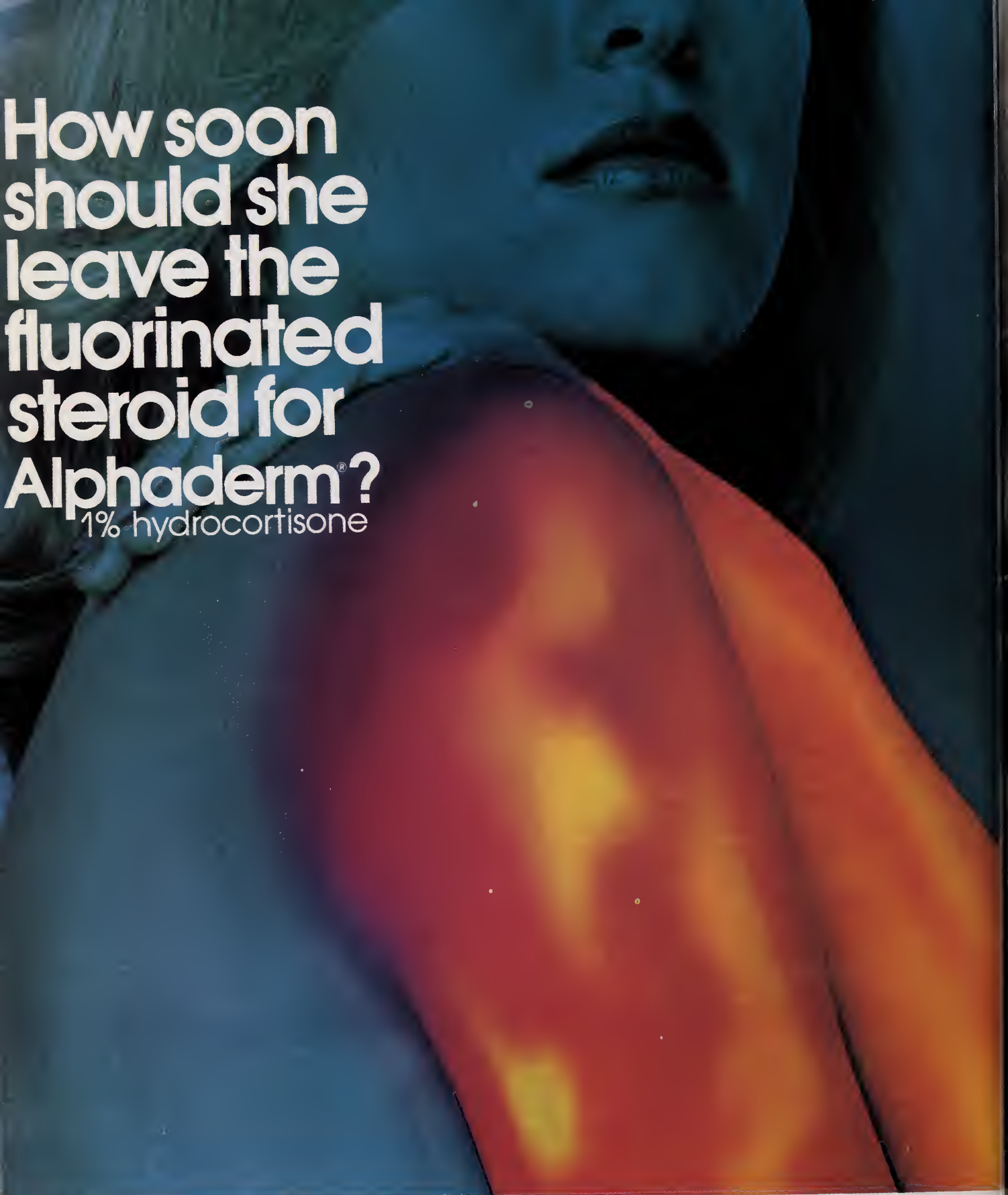
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venido desde la otra sala a buscarlo.

Toda esta maniobra se hace en el menor tiempo posible para reducir a un mínimo el tiempo de isquemia.

Toda la disección se hace retroperitoneal - esto conlleva un período más corto de ileo y por consiguiente de estadía postoperatorio en el hospital.

Una vez el donante es dado de baja se sigue en la clínica ambulatoria como cualquier otro paciente operado observando con mayor énfasis su función renal.

Hasta junio de 1979, de un total de 36 donantes vivos han ocurrido cuatro complicaciones, todas menores, dando un promedio de 11 por ciento. Esta cifra compara favorablemente con las de los mejores centros de trasplante en los Estados Unidos.

Las cuatro complicaciones que ocurrieron, todas en pacientes distintos, fueron las siguientes:

1. Pneumotorax pequeño (15 por ciento): tratado con aspiración.
2. Absceso de sutura: tratado con la remoción de la misma.
3. Arritmia cardíaca intraoperatoria: tratada con drogas antiarrítmicas.
4. Infección urinaria: tratada con antibióticos.

Todos estos pacientes recuperaron en su totalidad y están al presente igual que antes de someterse a la nefrectomía.

Por todo lo antes mencionado y debido a los buenos resultados obtenidos y tan poco riesgo envuelto es que se prefiere un donante vivo.

Donante Cadaver

Un candidato a trasplante que no tenga

donante vivo pasa a la lista de espera de riñón de cadaver. En esta lista se mantiene el nombre, dirección y teléfono, tipo de sangre y tejido de todos los pacientes en espera de que aparezca un paciente con muerte cerebral que reúna los criterios como donante y su familia inmediata acceda a la donación.

Requisitos para poder obtener un riñón de cadaver:

Muerte neurológica con apnea espontánea.

Edad límite 65 años.

Ausencia de sepsis sistémica.

Ausencia de malignidad generalizada, excepto del sistema nervioso central.

Ausencia de enfermedad renal.

Mantenimiento de función estable cardiovascular, pulmonar-ventilatoria, y renal hasta el momento de la nefrectomía.

Consentimiento a la donación por parte de la familia inmediata.

Criterios para declarar muerte neurológica:

Ausencia de movimientos espontáneos.

Apnea espontánea por un período prueba de 4 minutos.

Ausencia de reflejos del tallo cerebral, tales como:

- a. pupilas dilatadas y fijas.
- b. ausencia de reflejos corneales.
- c. ausencia de reflejo cilioespinal.



FIGURE 2

- d. ausencia de reflejo laríngeo.
- e. ausencia de función vestibular al estímulo calórico.

Estado arriba antes mencionado por espacio de 12 horas. La muerte cerebral existe únicamente si la condición patológica que produjo lo arriba mencionado es irreparable con

medios que tenemos al presente.

Tan pronto se tiene conocimiento de un posible donante que reúna todas las condiciones - en cualquier hospital de la isla - se traslada un equipo médico y paramédico para verificar los datos, y de ser aceptable el riñón, practicar la nefrectomía. Esto se lleva a cabo en el quirófano del hospital envuelto.

Tenemos máquinas de preservación de

riñón que mantienen a este una vez extirpado en casi perfecto estado por espacio de hasta 72 horas. Una de las máquinas de preservación es portátil, corrida por baterías, y se usa para el transporte del riñón hasta nuestro hospital o a cualquier otra parte fuera de Puerto Rico (Fig. 2).

Una vez que aceptamos al donante se le determina grupo sanguíneo y composición genética tisular. Esta información se coteja con nuestra lista de pacientes en espera de riñón. De encontrar algún paciente que sea

histocompatible, a este se le notifica de inmediato para que se reporte a nuestro hospital para efectuar el trasplante. De no tener ningún candidato en nuestra lista se cotejan las listas de los Estados Unidos por medio de una computadora. Si se encuentra algún candidato en los Estados Unidos y su hospital acepta el riñón - este se envía inmediatamente por avión en la máquina de preservamiento. De igual forma recibimos aquí riñones de Estados Unidos.

THE ROLE OF HLA IN TRANSPLANTATION AND THE HLA COMPOSITION OF THE PUERTO RICAN POPULATION

E. Nettleship, MS, MT

When a patient becomes a candidate for transplantation one of the first questions is "What is his HLA type" -- his *Human Lymphocyte Antigen* profile or more specifically his *Histocompatibility Linked Antigens*. The reason for this emphasis on tissue compatibility is that whenever a foreign substance penetrates the body's defenses the body tries to destroy it. For this reason the body attacks and rejects transplanted organs. The basis for this rejection is the recognition of "foreignness". The more similarities there are between donor and recipient, less "foreignness" or differences will be recognized, less immunosuppression is needed for graft acceptance and the survival of organs is improved.

How and where are these differences recognized? If we take two strains of mice - A and B - and a strain A mouse receives a skin graft from another strain A mouse, no differences are recognized and the graft is accepted as "self". If a strain B mouse receives a skin graft from the strain A mouse, tissue differences are recognized and the graft is rejected in 10 to 14 days. Moreover, if a strain B mouse receives the graft from the strain A, and lymphocytes are transferred from the first animal which previously rejected the graft, then there is an accelerated

rejection, now in 5 to 7 days. Thus lymphocytes are primarily involved in graft recognition and rejection, and in cell mediated immunity.

Histocompatibility antigens are present on all nucleated cells of the body and also on platelets. These antigens interact with immunocompetent cells and this reaction is mediated by receptors on the cell surface.

The HLA system is extremely complex and consists of many closely related genes on chromosome 6. The most studied genes are found in the A, C, B and D loci, known as the major histocompatibility complex (MHC). These genes are inherited codominantly as a unit and this unit is designated as a haplotype (one chromosome). So that in the normal inheritance pattern there are one each ACBD genes, or one haplotype, inherited from each parent. The HLA system is highly polymorphic, perhaps the most polymorphic genetic system known in man. Many alleles have been identified for each loci vs: A, 20; B, 31; C, 6; D, 11; Dr, 7. Frequencies of these antigens varies in different populations in different parts of the world. Also correlations have been found between certain specificities and a number of diseases.

The present study of the Puerto Rican population was done to find similarities or differences with other ethnic groups and to identify possible markers for disease associations with HLA specificities. By HLA typing of 453 individuals we determined the antigens of the A and B loci that are present in our population,

TABLE I

HLA - A and B - Antigen Frequencies (Per Cent) (1, 2)

Population	Puerto Rican	Mexican	Europeans	Indians	Japanese	Afr. Blacks	Amer. Cauc.	Middle Easterns	Amer. Indians	Mongo- loids
HLA - A1	11	12	31	23	3	8	32	24	2	4
A2	42	54	48	28	45	34	49	36	73	33
A3	15	10	28	14	3	15	22	19	2	2
A9	33	30	18	27	58	24	17	34	44	66
A10	18	18	12	14	17	15	13	10	--	14
A11	9	8	12	33	24	2	8	12	2	24
A28	7	16	8	12	6	17	11	12	17	4
A19	36	43	26	26	14	65	28	32	27	20
HLA - B5	26	10	12	34	34	4	11	28	19	17
B7	12	15	24	10	11	18	23	6	2	4
B8	6	7	21	15	1	7	20	6	--	2
B12	27	20	29	19	15	16	24	17	2	6
B13	4	4	4	4	5	4	6	6	--	8
B14	10	12	8	--	2	9	11	8	2	--
B18	6	6	10	4	2	10	9	10	2	6
B27	5	4	8	4	4	1	8	4	6	6
BW15	10	4	12	15	14	6	7	2	26	29
BW16	6	19	8	2	7	4	12	12	23	8
BW17	18	2	8	15	4	33	7	10	2	4
BW21	8	8	4	2	3	2	4	17	8	--
BW22	5	1	6	6	16	1	5	6	--	24
BW35	20	33	19	23	19	14	17	24	4	12
BW40	11	12	12	12	31	2	12	8	8	4

then calculated the percentage (frequency) of each antigen in the total number of typings. These frequencies were then compared with other populations. Table I shows the comparisons after analysis. We found a striking similarity (43 per cent) with the Mexican population. There is a strong (35 percent) European influence and the relatively high frequencies of A19, (36 percent) and BW17 (18 percent) demonstrates genetic influence from African Blacks. There are fewer similarities with Indians (India) and Japanese (30 percent), African Blacks and American Caucasians (22 percent), and American Indians and Mongoloids (9 percent).

However, these similarities are still less than 50 percent, so that there is a unique genetic pattern in the Puerto Rican population.

We also found relatively high frequencies with specificities that have been associated with certain diseases, namely B12-27 percent, BW17-18 percent, B5-26 percent, and A19-36 percent. There were no very low frequencies.

These findings are relevant in organ sharing since the immediate goal of histocompatibility testing is to minimize genetic disparity between donor and recipient. We may possibly have

better results by using donor kidneys from within our own population until we are able to match for the presumably more important D/Dr system.

A high incidence of certain diseases may be predicted from the high frequencies of: B17 associated with psoriasis arthritis, psoriasis vulgaris and non-specific psoriasis; B5 associated with Behcet's disease, ulcerative colitis and Hodgkin's disease; and B12 associated with Alopecia Areata. (2)

Although great progress has been made particularly in the last ten years we still do not know the complete anatomy and physiology of the MHC. Recent analysis of the D region appears to define part of the immune-reactivity-complex and will have an impact on understanding our defenses against disease.

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¿AUMENTA LA ISQUEMIA LA ANTIGENICIDAD DE UN ORGANO?

Magda Sofía Rodríguez, MS IV y Eduardo A. Santiago Delpín, MD

Muchos son los factores, algunos conocidos y otros no, que modifican los resultados de los trasplantes clínicos de riñón. Una de las áreas de más controversia en la literatura mundial está relacionada al efecto de la isquemia, con la resultante necrosis tubular aguda, en los resultados a largo plazo después de un trasplante de riñón. Algunos investigadores (1, 2, 3, 4) han observado que existe una mayor pérdida de riñones a largo plazo debido a rechazo en aquellos riñones que sufren la injuria de necrosis tubular aguda que en aquellos riñones que no tienen esta complicación. En particular, Santiago-Delpín y otros observaron que la pérdida era principalmente a largo plazo y debido a rechazo inmunológico; en su serie se habían eliminado ya aquellos riñones perdidos en etapas tempranas secundario a la injuria del riñón. No obstante, otros investigadores (5, 6) han presentado estudios en los cuales no se nota cambio alguno en la pérdida de riñones después de necrosis tubular aguda e isquemia.

Observación pertinente es también el que hacer un tumor experimental necrótico suele resultar en un aumento en su antigeni-

cidad. De ahí, parte de la explicación del éxito que muchas veces vemos al destruir tumores con radioterapia, ultrasonido, hipertemia, criocirugía, y en algunos casos isquemia de la lesión.

Nos preguntamos, entonces, ¿puede resultar la isquemia de un órgano en un aumento de su antigenicidad? De ser así, se daría peso a las observaciones discutidas anteriormente y nos obligaría a aumentar todos los esfuerzos posibles para proteger los riñones antes del trasplante de manera que se minimizara el riesgo de que se desarrolle isquemia y necrosis tubular aguda. Yendo más allá, se nos plantea como posible la hipótesis de que isquemia *in situ* pueda ser una causa de autosensibilización. La relevancia de esto en relación a enfermedad auto-inmune es evidente.

Fue nuestro propósito entonces, el identificar autosensibilización después de un período de isquemia en diferentes órganos. La fase II de estos experimentos se está llevando a cabo actualmente y consiste en identificar un aumento en sensibilización en un modelo de alo-trasplante.

Materiales y Métodos

Modelo Experimental:

Los experimentos que se presentan son parte de una investigación sistemática de isquemia en diferentes órganos. Incluyen nuestros experimentos

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isquemia de un lóbulo hepático en la rata; isquemia de riñones en rata, conejo, y ratón; e isquemia de una extremidad en el conejo. Tan solo presentamos el resultado de los experimentos de isquemia en el riñón.

Ratas salvajes ("outbred") fueron anestesiadas con Pentobarbital intraperitoneal. Al momento de la inducción se le inyectaba además Heparina 1mg/kg intraperitoneal. Se practicó una laparotomía mediana con identificación del riñón izquierdo. Disección meticulosa utilizando instrumentos de microcirugía se llevó a cabo para aislar las estructuras vasculares del riñón izquierdo, teniendo muchísimo cuidado de identificar y no causar daño al sistema excretor. Utilizando una minúscula pinza de hemostasis, se ocluyeron ambas arteria y vena por un período de 15 minutos. Al momento de la oclusión, y como índice de una oclusión total, el riñón se tornaba en breves instantes pálido, y luego moteado y cianótico. Se cerró la laparotomía, y 14-28 días después se sacrificó al animal removiendo rápidamente ambos riñones, derecho e izquierdo, congelándolos inmediatamente y haciendo cortes pertinentes para inmunofluorescencia, microscopía de luz y microscopía electrónica.

La microscopía de luz se hacía con tinción de hematoxilina y eosina. Los cortes por congelación para inmunofluorescencia fueron incubados con inmunoglobulina anti-cadena anti-rata obtenidos de los Laboratorios Cappel. Se usó este material sin diluir. Los controles eran ratas en las cuales no se le practicó isquemia del riñón izquierdo.

Resultados

Todos los animales sobrevivieron.

Al momento del sacrificio y autopsia, ambos riñones aparentaban ser normales.

Al examen microscópico de luz, ambos riñones se veían completamente normales sin evidencia de necrosis tubular aguda.

En animales con isquemia de un riñón, ambos riñones fluorecían brillantemente bajo el microscopio de luz ultravioleta. El brillo era lineal y se depositaba principalmente en los glomérulos y esporádicamente en la mem-

brana nasal de los túbulos. Aquellos animales que no sufrieron isquemia, no demostraron brillo alguno.

Conclusiones

Estos experimentos son nuevos y de naturaleza preliminar. Se están llevando a cabo experimentos para tratar de duplicar estos resultados preliminares, no solo en la rata sino en otros roedores también. Como conclusión tentativa, sugerimos que la isquemia puede inducir la formación de anticuerpos que reaccionan con el riñón. De poder confirmar esta información, podríamos adelantar la hipótesis de que puede ser éste un factor en algunas enfermedades auto-inmunes.

Agradecimiento

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patients in hot weather. Hyperuricemia may occur or gout be precipitated in certain patients. Insulin requirements in diabetic patients may be increased, decreased, or unchanged and latent diabetes mellitus may become manifest. Chlorthalidone and related drugs may increase the responsiveness to tubocurarine. The antihypertensive effects of the drug may be enhanced in the postsympathectomy patient. Chlorthalidone and related drugs may decrease arterial responsiveness to norepinephrine. If progressive renal impairment becomes evident, as indicated by a rising nonprotein nitrogen or blood urea nitrogen, a careful reappraisal of therapy is necessary with consideration given to withholding or discontinuing diuretic therapy. Chlorthalidone and related drugs may decrease serum PBI levels without signs of thyroid disturbance.

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It Takes Time To Take Off Pounds

Dieting Is Slow

For most overweight persons, there is no medical justification for rapid weight loss or a nutritionally imbalanced diet.

A good weight-reduction program is one that is reduced in calories and adequate in nutrients. Regular meals and the Four Food Groups form the basis of a good diet that is suitable (or adaptable) for people with different health problems.

The individual who needs a diet low in saturated fat and cholesterol, for example, should continue to use milk products in the recommended amounts because of their high nutritive value, but should always choose nonfat products from this group.

There aren't any "reducing foods," a new American Medical Association pamphlet says. When you lose weight, it's because of taking in fewer calories than you are burning. Total calories, not the foods they come from, make

the difference. Bear in mind, though, that fats are the most concentrated source of calories. One gram of fat contains nine calories, compared with four calories per gram of either protein or carbohydrate and seven calories per gram of alcohol.

If you are more than eight or ten pounds overweight, it's unrealistic to think you will solve the problem in two or three weeks. Weight lost through crash diets almost always is regained when normal eating patterns are resumed.

Reducing salons and health clubs are fine, if you can afford them. Group workouts may give moral support, but you can exercise just as well at home. Exercise machines that pretend to shake it off without effort on your part are a waste of time and money.

As to protein supplements, save your money. Most people get all the protein they need from ordinary foods. There are a number of drugs that have been misused in weight-reducing programs. Use of drugs in weight control is rarely or never justifiable, says the AMA pamphlet.

Diet clubs, such as Weight Watchers and TOPS, can help many individuals gain control of their eating habits.



April, 1979

Frank Chappell
Science News Editor
AMA

¿MODIFICA EL HIGADO LA ANTIGENICIDAD DE UN ORGANO?

Manuel H. Castillo, MD, Eduardo A. Santiago Delpín, MD y Esteban Moreno, MD

Quizás el problema más importante con el cual se confronta el médico que trabaja con trasplantes es la forma en que el organismo maneja los tejidos injertados que se obtienen de un donante cuya composición genética es distinta de la del huésped. Se han desarrollado maneras múltiples de bregar con el mecanismo de rechazo, pero todas tienden a alterar de una manera sustancial la inmunocompetencia del huésped, haciéndolo susceptible a problemas de infección y tumores, entre otras complicaciones. Por esta razón la experimentación en trasplantes es muy grande ya que se trata de obtener una manera eficaz de vencer el rechazo sin eliminar del todo las defensas inmunológicas del organismo.

Recientemente algunas observaciones han hecho pensar que el hígado puede de alguna manera modificar la antigenicidad de los tejidos. Observaciones pertinentes incluyen: (a) a algunos antígenos administrados por vía oral son tolerogénicos (1) en vez de inmunogénicos; (b) islotes de células pancreáticas inyectados intraesplénico o intraportal sobreviven por mayor tiempo que aquellos que se implantan por vía sistémica (2); (c) los trasplantes de hígado son menos inmunogénicos y la

respuesta de rechazo suele ser menor que la de otros órganos (3); (d) trasplante de paratiroides dentro de la sustancia del hígado se rechazan con menor vigor inmunológico (4); (e) incubación de antígeno con membrana de célula hepática, lo puede convertir en tolerógeno (5). Estas observaciones nos motivan a cuestionarnos si algún grado de modificación de los antígenos es responsable de esta aceptación inmunológica.

Diseño del Experimento

La idea de este experimento era utilizar en primer lugar un antígeno más complejo que los previamente estudiados en la literatura, y por esta razón seleccionamos injertos de piel. La segunda razón era comparar la sobrevivencia del tejido injertado en localizaciones anatómicas cuyo drenaje venoso era hacia el hígado. Injertos alogénicos de piel fueron entonces puestos en la parte dorsal de la caja torácica de ratones, sobre la superficie de un riñón, sobre la superficie del bazo, del estómago o del hígado.

Materiales y Métodos

Usamos ratones de las cepas C3H, CBAJ, BALB/C, de aproximadamente tres meses de edad y pesando entre 20 y 25 gramos. El animal donador se sacrificó utilizando anestesia de éter, y se preparó piel de la cola después de limpiarla apropiadamente, cortándola en

Del Laboratorio de Cirugía Experimental, Departamento de Cirugía; Departamento de Patología; Universidad de Puerto Rico; y Departamento de Cirugía, Hospital de Veteranos, San Juan, Puerto Rico.

TABLA I

Parámetros Histológicos de Rechazo

-
1. *Infiltración celular.*
 2. *Destrucción parcial limitada a epidermis.*
 3. *Destrucción de la epidermis.*
 4. *Necrosis de la dermis.*
 5. *Destrucción incluyendo glándulas sebáceas.*
 6. *Infiltración de células gigantes, preservación solo del pelo.*
-

pequeños cuadros de menos de un centímetro cuadrado. El recipiente se durmió con anestesia de éter y en un primer grupo control compuesto de veinte ratones de cepa diferente a la del donante se le excindió parte de la piel de la caja torácica izquierda, lugar en el cual se le posicionaba delicadamente el cuadrado de piel de la cola del donador. Se cubrió la piel con gasa vaselinada y yeso por un período de ocho días. Luego se removió el yeso y se observó la piel diariamente para evidencia del rechazo. Todos los grupos subsiguientes sufrían bajo anestesia general una laparotomía y, dependiendo del grupo, cada uno de veinte ratones sufría una disección del riñón, del bazo, o del estómago y se injertaba una pequeña porción de piel encima de cada uno de estos órganos fijándolo en su sitio con una o dos suturas de polipropileno 6-0.

Del día post operatorio 14 en adelante se sacrificaban varios animales cada tres días hasta los 30 días. El órgano a donde se había trasplantado la piel

se removía y se fijaba en formalina para estudio de microscopio de luz. Los criterios del examen macroscópico incluían el grado de inflamación y la presencia de tejido viable a simple vista. Los criterios de viabilidad al examen microscópico eran cuantificados de acuerdo a la escala que se ilustra en la Tabla I.

Resultados

En todos los animales cuyo trasplante se hacía sobre el bazo, se encontró piel aparentemente normal a simple vista hasta el día 60. Incluía esto la presencia de vello visible. La piel trasplantada encima del hígado o del riñón solía ser más fina y blanda que aquellas trasplantadas encima del bazo o del estómago.

Al examinar microscópicamente estas muestras se encontró que había infiltración

celular ya en el día 14, grados 1, 2, 3 (Tabla I), en todos los grupos estudiados irrespectivo del lugar. Hacia el día 30 después del injerto, variaba el grado de infiltración, de rechazo y de necrosis, pero se encontraba mejor conservada la arquitectura del injerto en los grupos injertados en el estómago o en el bazo que aquellos encima del hígado o del riñón (Grado 4 vs 5 y 6; $P < 0.05$).

Comentarios

Cuando se trasplanta un órgano a un huésped alogénico, el sistema inmunológico se activa de manera que el órgano trasplantado se reconoce, el huésped se sensitiza, y una reacción inflamatoria parcialmente específica pero eventualmente inespecífica y de grado muy intenso, se establece hacia el órgano hasta que es destruido. Experimentos recientes sugieren que el hígado puede alterar la inmunogenicidad de algunas sustancias injertadas por vía oral o injertadas por la ruta portal. Ejemplo de esto son nuestros datos preliminares según aquí presentados que sugieren que sistemas de antígenos más complejos tales como los tejidos de piel pueden comportarse de manera diferente si se trasplantan sobre órganos que drenen al hígado vis-a-vis que sobre órganos que drenen sistémicamente. Aunque esta data es preliminar, promete arrojar cierta luz sobre mecanismos de sensitización. De

comprobarse esta hipótesis podríamos entre otras cosas reconsiderar el lugar en el que actualmente colocamos algunos de los trasplantes, y así mismo sugeriría una vía de pre-tratamiento con antígenos antes del trasplante.

Agradecimiento

Los autores agradecen la valiosa ayuda durante estos experimentos de Yolanda Padilla, Benjamín Dieppa, Manuel Caloca, Luis Román, Jorge Oliver, Mildred Ramírez y Juan A. Ramírez Sánchez.

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RESULTADOS DEL PROGRAMA DE TRASPLANTE RENAL DE PUERTO RICO

E. A. Santiago Delpín, MD

El Programa de Trasplante de Puerto Rico es una operación combinada, en la cual participan un gran número de profesionales médicos y paramédicos. Esta actividad se ubica en el Hospital de Veteranos y sirve a pacientes veteranos y a un número limitado de pacientes no-veteranos. Comenzamos nuestras actividades oficialmente en enero del 1977, y en esos tres años se han llevado a cabo 50 trasplantes de riñón, de los cuales 47 se presentan en este manuscrito.

De estos 47 pacientes, 14 son veteranos y 33 son no-veteranos; 33 son varones y 14 mujeres. Las causas de la enfermedad renal que llevó al paciente a necesitar un trasplante son parecidas a las que se informan en series grandes, e incluyen: glomerulonefritis, nefritis familiar, pielonefritis, uropatía obstructiva en particular en los niños, y un paciente con púrpura de Schonlein-Henoch. El paciente más joven tenía 7 años en el momento del trasplante y el paciente más viejo, 57 años. La mayoría de los pacientes es de edad mediana, entre los 15 y 45 años, con tres niños y nueve personas sobre 45 años.

La Tabla I ilustra el tipo de donante que se ha utilizado. Se puede observar que la mayoría son pacientes familiares y se prefiere estos pues la afinidad genética hace que

los resultados sean mejores. Nos agrada el confirmar que hemos tenido 8 pares de donantes-recipientes idénticos en 19 hermanos, lo cual mejora en gran medida los resultados de trasplante y a la vez facilita el manejo de inmunosupresión.

La selección del donante-recipientes ha sido discutida ya en ocasión anterior (1), pero, brevemente, se prefiere utilizar un donante en perfecto estado de salud y que sea afin genéticamente con su recipiente. El recipiente tiene muy pocas restricciones de selección y tan solo excluimos aquellas personas que tienen cáncer generalizado incurable, infección generalizada, o enfermedad hepática avanzada. Se utiliza el riñón izquierdo preferiblemente por el largo de su vena, o aquel riñón que tenga una sola arteria. El riñón se implanta con técnica operatoria standard en los vasos ilíacos del lado derecho del paciente. Como regla general, solemos ver función del riñón casi instantáneamente.

La Tabla II ilustra nuestros resultados de sobrevida. Se puede notar que la sobrevida del paciente es muy buena, al igual que la del riñón, y compara favorablemente con las series grandes de Norte América y de Europa. La función es prácticamente normal en la mayoría de los casos con 80 por ciento de los pacientes teniendo una creatinina estable en menos de 2 mg/dl, y 20 por ciento con una creatinina de 2.0 o mayor/dl.

La rehabilitación de estos pacientes se discute en una sección aparte, pero se quiere enfatizar que 66 por ciento de los pacientes tienen una rehabilitación total a largo plazo,

De la Unidad de Trasplante, Servicio de Cirugía, Hospital de Veteranos, San Juan, Puerto Rico.

TABLA I

Tipo de Donador

<i>Padre a Hijo</i>	<i>14</i>
<i>Hijo a Padre</i>	<i>3</i>
<i>Hermano</i>	<i>19</i>
<i>Idéntico</i>	<i>8</i>
<i>No-Idéntico</i>	<i>11</i>
<i>Sobrino</i>	<i>1</i>
<i>Cadáver</i>	<i>10</i>

TABLA II

Sobrevida (Curva Actuarial)

	<i>1 AÑO</i>	<i>2 AÑOS</i>
<i>Sobrevida de Pacientes</i>	<i>93 por ciento</i>	<i>89 por ciento</i>
<i>Sobrevida de Riñones</i>	<i>93 por ciento</i>	<i>83 por ciento</i>

entendiéndose por esto que se ha reintegrado todas las esferas de funcionamiento, incluyendo trabajo; y que el 34 por ciento sobrante desarrolla una rehabilitación parcial con gran potencial de rehabilitación total.

A pesar de estos resultados, nos confrontamos con una variedad de complicaciones que demandan atención pronta y certera ya que de no establecerse un diagnóstico muy

rápido, se empeliga la viabilidad del riñón o la vida del paciente. En particular, es crítico el diagnosticar los episodios de rechazo que ocurren en estos pacientes de manera que se puedan tratar rápidamente. Es importante identificar que se han observado 35 episodios de rechazo en 22 pacientes con pérdida de tan solo 3 riñones; de éstos, 2 por rechazo agudo y 1 por rechazo acelerado. La inmensa

TABLA III

Infecciones

<i>Infecciones Urinarias</i>	<i>16 episodios en 8 pacientes</i>
<i>Prostatitis</i>	<i>8 episodios en 7 pacientes</i>
<i>Herpes Zoster</i>	<i>6 episodios en 6 pacientes</i>
<i>Herpes Encefalitis</i>	<i>1 episodio en 1 paciente</i>
<i>Neuralgia Post-Herpética</i>	<i>1 episodio en 1 paciente</i>
<i>Pulmonía por Pneumococo</i>	<i>1 episodio en 1 paciente</i>
<i>Pulmonía por Citomegalovirus</i>	<i>2 episodios en 2 pacientes</i>
<i>Pulmonía por Strongyloides</i>	<i>1 episodio en 1 paciente</i>
<i>Pulmonía por P. Carinii</i>	<i>1 episodio en 1 paciente</i>
<i>Abceso Pulmonar Anaeróbico</i>	<i>1 episodio en 1 paciente</i>
<i>Micobacteriosis</i>	<i>2 episodios en 2 pacientes</i>
<i>Sepsis por Listeria</i>	<i>1 episodio en 1 paciente</i>
<i>Hepatitis por Toxoplasma</i>	<i>1 episodio en 1 paciente</i>
<i>Strongyloidiasis</i>	<i>5 episodios en 4 pacientes</i>
<i>Giardiasis</i>	<i>1 episodio en 1 paciente</i>
<i>Candidiasis Oral</i>	<i>5 episodios en 5 pacientes</i>
<i>Esofagitis por Candida</i>	<i>2 episodios en 1 paciente</i>
<i>Hongo Cutáneo</i>	<i>8 episodios en 6 pacientes</i>

mayoría de los episodios de rechazo son reversible con la terapia apropiada, y el corolario es que este manejo depende prácticamente y exclusivamente de cuán temprano y rápido sea manejado el episodio de rechazo. Igual de importante es la observación que no se ha observado episodio de rechazo alguno en 15 pacientes, 7 de los cuales son idénticos, pero los restantes no lo son.

De importancia en el diagnóstico diferencial son las complicaciones técnicas que pueden ocurrir en estos pacientes, las cuales

se resuelven con terapia apropiada y no con la terapia de inmunosupresión que se usa para el rechazo. Hemos observado dos episodios de necrosis tubular aguda en pacientes de trasplante vivo, 4 pacientes con linfocitos que han requerido tratamiento quirúrgico, 1 paciente con obstrucción ureteral e hidronefrosis, y 1 paciente con necrosis de su uréter y pelvis renal. Corrección quirúrgica ha resultado en cura de las complicaciones en todos los casos.

El problema de las infecciones sigue sien-

do un problema muy severo y nuestra casuística es prácticamente paralela a aquellas de series de Norte América y de Europa. Hemos encontrado infecciones relacionadas a organismos intracelulares o a organismos de baja antigenicidad. El listado de estas complicaciones se ilustra en la Tabla III. La mayoría de estas infecciones son potencialmente letales y en particular las complicaciones pulmonares llevan una tasa de mortalidad muy alta. Hemos logrado disminuir esta mortalidad en gran medida debido a la agresividad con la cual se diagnostica al paciente que se ve críticamente enfermo o que demuestra evidencia de infección o fiebre. Las causas de muerte en nuestros pacientes han incluido pulmonía por *Klebsiella*, pulmonía por strongyloides, infección y obesidad, embolia pulmonar, coma hepático, e infarto cardíaco.

En resumen, nuestro Programa presenta los mismos problemas de infecciones que en otros centros grandes de trasplante. Sin embargo, nos alegra mucho la observación de que vemos rechazo con una incidencia menor a la que se observa en la población general de pacientes trasplantados, y le atribuimos a esto la homogeneidad genética que tenemos en nuestra población. Este punto en particular se discute en el papel de Nettleship en este mismo volumen. En adición a esto, en particular con los pacientes en espera de trasplante de cadáver, se ha alterado la política del Programa de manera que recibe transfusiones de sangre preoperatoria. Ha sido motivo de gran estudio y discusión en los últimos 8 años el uso de transfusiones de sangre pretrasplante en el caso del candidato a riñón de cadáver, pero los datos de todos

los estudios son suficientemente consistentes para obligar a un cambio de política en esta área en particular. Nuestros pacientes en espera de riñón de cadáver en este momento reciben por lo menos 5 transfusiones de sangre antes de ser activados en la lista de espera de la computadora. El énfasis durante el próximo año incluirá trasplante de cadáver, de manera que se pueda estudiar el efecto de este cambio en política en nuestros pacientes (2).

Se sigue viendo actividad significativa en todos los centros de trasplantes del mundo. Está va dirigida a encontrar mejores maneras de inmunosuprimir al paciente sin eliminar por completo sus defensas en contra de las infecciones. El deseo de todos es el poder eliminar drogas nocivas, como la azatioprina y los esteroides. Los avances recientes en tipificación para lugares genéticos de importancia a la respuesta inmune, como lo es el D y Dr en el ser humano, también ayudarán a establecer mejores pares de donantes y recipiente. En general, el horizonte de la próxima década se ve mucho más claro que anteriormente ya que disponemos de mucho más conocimiento del comportamiento del sistema inmunológico y sus componentes.

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RADIONUCLIDE STUDIES IN THE EVALUATION OF RENAL TRANSPLANTS

Julio V. Rivera, MD and Eduardo Santiago Delpín, MD

The evaluation of individual renal function by radionuclide techniques was first proposed by Taplin in 1956 (1). Since that time considerable refinement of these has been possible as a result of the introduction of new radiopharmaceuticals, improved sensitivity and resolution of detection instruments and the availability of data processing equipment. Because of the non-invasive nature of these examinations and the virtual absence of untoward effects, these procedures have been found to be especially suitable for the study of renal function and the detection of complications in renal transplant recipients (2).

The present study is a review of our experience in the transplant program in Puerto Rico.

Material and Methods

A retrospective study was made of all studies performed on renal transplant patients since the start of the program in 1976.

Renograms were performed following the administration of 10-30 μ Ci of ^{131}I orthodihydroxyisotriphosphate.

A sodium iodide detector over the upper third of the organ recorded a graph of renal activity, avoiding as much as possible the effect of radioactivity in the bladder. A second detector over the precordium recorded blood activity from 10 to 20 minutes after injection. The halftime of this curve was calculated graphically on semilogarithmic paper.

Renograms were classified as normal (I), delayed (II), or ascending (III) (Fig. 1).

Renal dynamic study was carried out in a scintillation camera following the administration of approximately 15 mCi of $^{99\text{m}}\text{Tc}$ diethylene triamine penta-acetic acid (DTPA). Data was recorded photographically or on video tape continuously during the first minute and intermittently for 1 to 2 hours (Fig. 2).

Clinical evaluation of each patient's progress and diagnosis of any ensuing complications was based on all available clinical and laboratory data and recorded by one of us (ESD). On the basis of this, the patient's course was classified as excellent, good-fair, or poor.

Results and Discussion

Review of the renograms on this group of patients revealed several findings which seem to be worthy of note.

Six renograms performed because of non-specific symptoms such as fever and general malaise which led to final diagnoses of non-renal disease were normal or unchanged when compared to earlier studies in the same patients.

From the Nuclear Medicine and Surgery Services, Veterans Administration Medical and Regional Office Center, and the University of Puerto Rico School of Medicine.

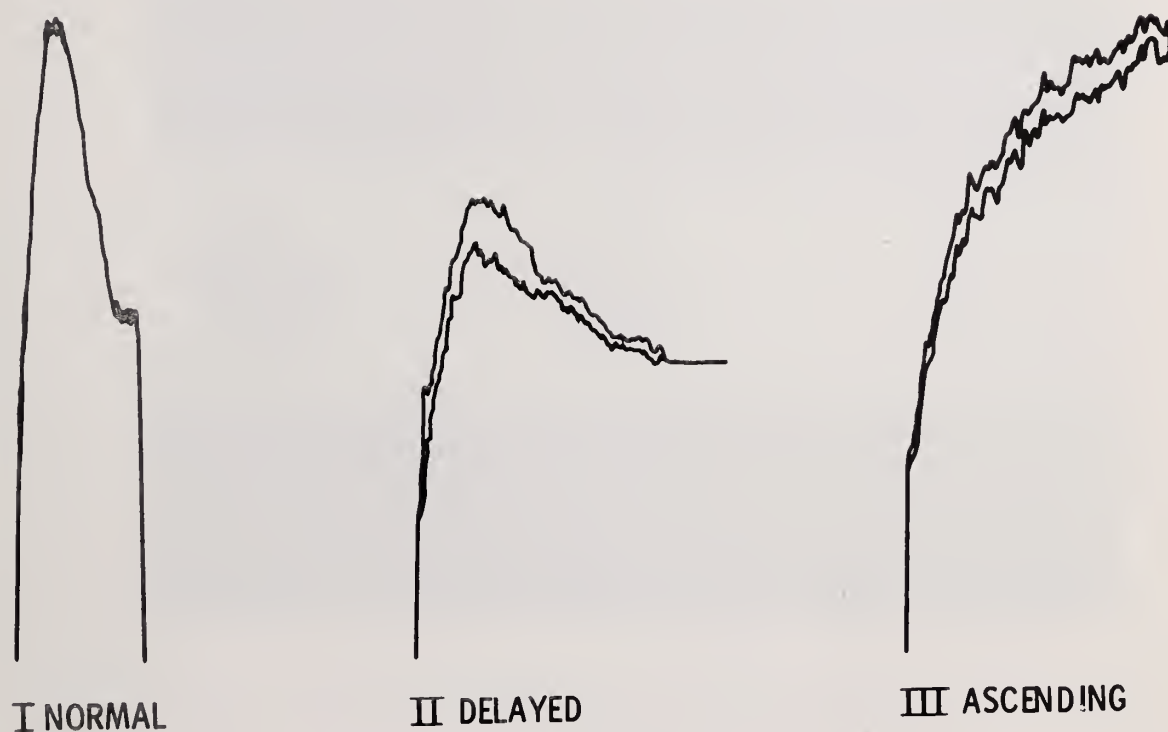


Fig. 1: Renogram patterns.

Thus, contrary to what has been found in other studies, the renogram in this small group was not affected by non-urolological disease. On the other hand, deterioration of the renogram pattern usually indicated an urolological problem and thus helped orient the diagnostic and therapeutic program. Because of its simplicity, absence of untoward reactions and extremely low radiation dose, the renogram may be repeated as often as necessary.

The data also appears to indicate that the renogram has prognostic value in renal transplant patients. When renograms performed past the immediate post-operative period were related to the long-term clinical

condition or outcome of the transplant procedure, it was found that a normal (Type I) study was usually associated with a good or excellent prognosis (Table I). Patients with various degrees of abnormality (Type II) followed a variable course. An ascending (Type III) curve was associated in most instances with a poor prognosis, frequently leading to loss of the kidney due to rejection or death related to a variety of complications (Table II). It is of interest that concurrent serum creatinine level in 5 of these patients was not higher than 2.5 mg/dl.

Table III summarizes the results of ^{99m}Tc DTPA dynamic studies in the detection of



Fig. 2: Normal renal dynamic study (^{99m}Tc DTPA) shows prompt visualization of renal transplant with the iliac artery.

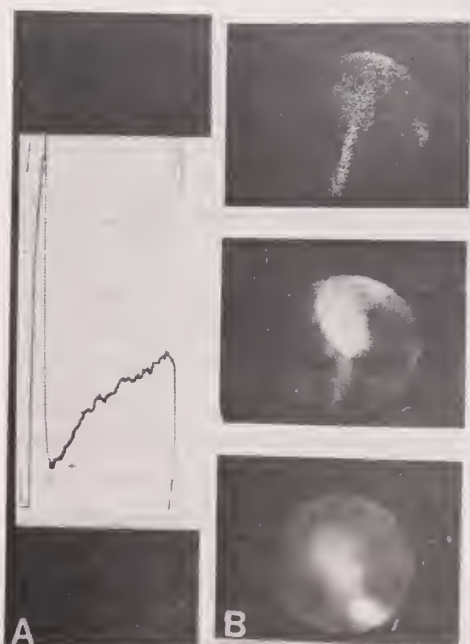


Fig. 3: Rejection. A. Ascending renogram curve. B. Delayed parenchymal distribution and prolonged retention of ^{99m}Tc DTPA. Similar findings may occur in acute tubular necrosis.

complications of renal transplant surgery. It is evident that this study is quite effective in the diagnosis of the most frequent problems seen in these patients, acute functional failure due to rejection or tubular necrosis and abnormalities in drainage. The method employed does not allow differentiation between tubular necrosis and rejection. The separation made between these two groups on Table III was arbitrary, being based solely on the time of onset of renal failure after operation. The single case of arterial obstruction was correctly identified. Although perirenal lymphocele may be identified, this is best confirmed by ultrasonography. Fig. 3 illustrates the usual renographic and ^{99m}Tc DTPA pictures seen in transplant rejection.

In summary, it may be stated that radio-nuclear studies are a valuable tool in the evaluation of function of transplanted kidneys and in the detection of surgical complications. We have presented evidence which indicates

TABLE I
Renogram - Prognosis

P A T T E R N			Outcome: Function
I	II	III	
5	----	----	Excellent
8	7	----	Good-Fair
----	3	11	Poor

$$X^2 = 31.46 \quad df = 4 \quad p = 0.001$$

Each number represents one or several renograms done in each patient.

TABLE II:
Type III Renogram - Patient Outcome

Renogram Time Post Transplant	Creatinine (mg/dl)	Diagnosis	Outcome
1. 59 days	1.4	Rejection	Chronic rejection, fair function
2. 51 days	1.0	Rejection; sepsis	Died, 70 days post trans- plant
3. 0-9 days	5.7	Rejection	Nephrectomy, 30 days post transplant
4. 7 months	1.7	Rejection	Died: sepsis, pancreatitis, chronic rejection
5. 30 days	3.2	Rejection	Nephrectomy, 40 days post transplant

6. 28 days	2.5	Rejection	Nephrectomy, 40 days post transplant
7. 67 days	5.2	Nephrotic syndrome	Poor function
8. 25 days	3.5	Rejection	Nephrectomy, 34 days post transplant
9. 30 days	3.0	Rejection	Nephrectomy, 46 days. Died, 57 days
10. 40 days	1.1	Urinary infection; rejection stomal prolapse	Good function

TABLE III

Renal Dynamic (^{99m}Tc DTPA) Study

Clinical Diagnosis	STUDY				RESULTS	Totals
	Normal	ATN	Rejection	Drainage Problem		
Normal	39	1	2	4		46
ATN*	1	10	---	---		11
Rejection	9	---	40	4		53
Drainage problem	2	---	---	7		9
External problem	10	---	---	---		10

* - Acute tubular necrosis was diagnosed arbitrarily on the basis of early onset of renal dysfunction.

that renograms may have prognostic value. Radionuclear studies are useful in the selection of patients in whom radiological examinations, renal biopsy, and instrumentation which carry known risks, are indicated.

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LISTA DE ANUNCIANTES

BOEHRINGER INGELHEIM
Catapres

BURROUGHS WELLCOME
Neosporin
Septra

Mc NEIL LAB.
Parafon Forte
Tylenol / Codeine

MERRELL-NATIONAL
Bentyl
Quinamm

NORWICH INTERNATIONAL
Alphaderm

ROCHE LAB.
Librium
Valium

SMITH, KLINE & FRENCH
Tagamet

SYNTEX LAB.
Neo-Mull-Soy

U. S. V. PHARM.
Hygroton 25

METABOLISMO DE CALCIO EN EL PACIENTE TRASPLANTADO: INFORME PRELIMINAR

Laura E. Lespier-Dexter, MD, A. Márquez, BS y N.Estepa, RN

El riñón es un regulador importante del metabolismo de calcio y fósforo; mantiene los niveles dentro de ciertos límites, activa la vitamina D circulante e indirectamente regula los niveles de hormona paratiroides circulante ya que la degrada. La disminución progresiva de función renal que resulta en insuficiencia renal terminal en un período variable induce ciertos cambios fisiológicos que al compensar algunas anormalidades resulta en otras (1) (Hipótesis de Trueque). Ejemplo de esta hipótesis son las anormalidades del metabolismo de calcio y hueso (2-3). Al disminuir la filtración glomerular se acumula el fósforo, aumento que resulta en una disminución del calcio iónico circulante. El calcio iónico bajo es el estímulo más potente para la secreción de hormonas paratiroides que moviliza el calcio óseo. Al hacerse persistente este estímulo las células paratiroides se hiperplasian y la secreción hormonal se fija a un nivel alto y resulta en movilización o resorción de calcio ósea persistentes. A largo plazo ocurren cambios de hiperparatiroidismo en el hueso (3). El riñón tiene

además un papel importante en la producción de Vitamina D activa (4). Al perderse parénquima renal se pierde la capacidad de activar la vitamina D comprometiendo así sus funciones propias como la absorción de calcio y fósforo a nivel gastrointestinal. Esto resulta en disminución del nivel de calcio, estímulo adicional para la secreción de hormona paratiroidea con los resultados óseos detrimentales. El hiperparatiroidismo secundario (2, 3, 7), resulta en cambios óseos semejantes a osteitis fibrosa quística, la deficiencia de vitamina D activa resulta en osteomalasia ambos se identifican en conjunto como osteodistrofia renal (3). (Fig. 1)

Hasta el presente las medidas terapéuticas disponibles solo logran controlar parcialmente el hiperparatiroidismo en los pacientes hemodializados crónicamente (5-8) y al momento del trasplante renal esperamos que un riñón funcional revierta toda anormalidad (9). Este retorno está en ocasiones retardado y la hiperplasia paratiroidea e hiperparatiroidismo secundario puede persistir, resultando en hipercalcemia, hipofosfatemia y deterioro de las estructuras óseas. Este fenómeno se ha reportado de un 2 a 25 por ciento de pacientes trasplantados.

Con el propósito de delinear el curso natural y recobro de función paratiroidea normal en nuestros pacientes con trasplantes de vivos se llevarán a cabo las presentes observaciones que resumiremos aquí en parte.

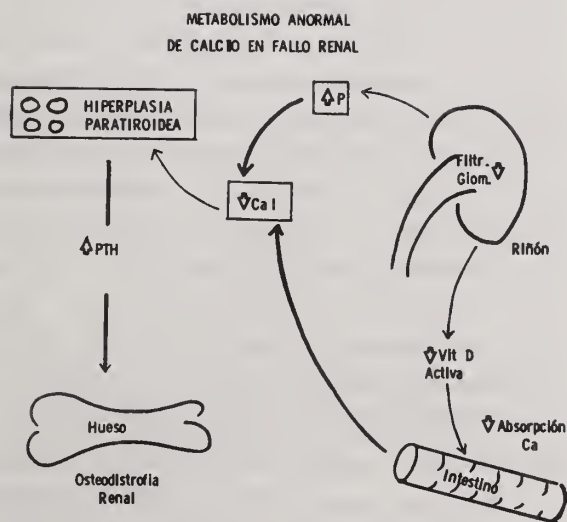


FIGURA 1

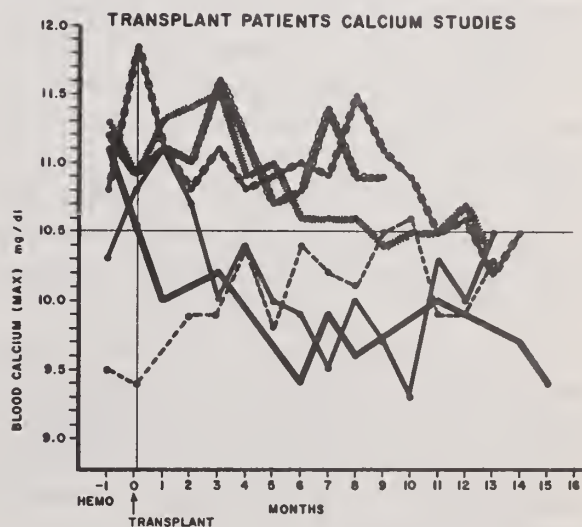


FIGURE 2

Pacientes y Métodos

Seis pacientes trasplantados con injertos de donantes vivos, compatibles, se evaluaron luego de transcurridos 9 a 15 meses de trasplante. Se analizaron las determinaciones de calcio, fósforo, creatinina y fosfatasa alcalina durante el último mes de hemodiálisis. Retrospectivamente se analizaron estos mismos valores luego del trasplante, específicamente se consideraron tanto los valores promedio de 4 semanas como los valores máximos de calcio. Las observaciones se hicieron en períodos durante los cuales no había evidencia de rechazo agudo. Cada paciente recibía dosis apropiadas de inmunoterapia (azathioprina y prednisona). Los niveles de fósforo se mantuvieron

normales mediante el uso de suplementos. Un paciente había sido paratiroidectomizado antes del trasplante debido a hipercalcemia persistente.

A todos los pacientes se le hicieron radiografías óseas antes del trasplante y al final del período de observación.

Resultados y Discusión

Durante el período de hemodiálisis cuatro pacientes evidenciaron valores de calcio mayores de 10.5 mg/dl (Fig. 2). Un paciente normocalcémico había sido paratiroidectomizado. Al

momento del trasplante, cuatro pacientes demostraban hipercalcemia, uno estaba en el límite y uno normocalcémico.

Luego del trasplante los 3 hipercalcémicos normalizaron sus valores de calcio; al tercer mes, al noveno y al undécimo mes. Un paciente persistió hipercalcémico durante todo el período de observación pero su curso de observación era aún corto. Un paciente normocalcémico mantuvo sus niveles de calcio pero desarrolló niveles elevados durante el duodécimo mes. Los promedios de función renal se mantuvieron estables durante los períodos de observación.

No hubo correlación significativa entre los valores de calcio luego de trasplante y edad, duración conocida de enfermedad renal o tiempo en diálisis, valores de calcio durante diálisis o antes de trasplante, o función renal del trasplante.

Ningún paciente demostró cambio en el análisis de la radiografía de hueso que fuera consistente con progreso de la osteodistrofia renal. Evaluación del análisis mineral de hueso por la técnica de absorción de fotones (Nerland-Cameron Bone Mineral Analyzer) se encontró bajo lo normal en solo un paciente; aquél con hipercalcemia persistente.

Estos resultados son consistentes con un estado de hiperparatiroidismo prolongado durante el período luego de un injerto exitoso, donde los valores de calcio elevados no resultan en una inmediata supresión de la secreción de hormona paratiroidea (no reportada aquí) que en condiciones normales mantiene los niveles séricos de calcio dentro de los límites apropiados. La intermitencia de la hipercalcemia es consistente con un grado de flexibilidad en la secreción hormonal paratiroide con posibilidad de servo-control. El tiempo que tomó a cada paciente el normalizar sus valores máximos de calcio, es varia-

ble, y probablemente refleja el grado de hiperplasia glandular. Aunque variable, los valores demostraban tendencia hacia lo normal.

Algunos informes han demostrado niveles de hormona paratiroidea normal de uno a cuatro meses luego de trasplante (10). Otros (11-12) reportan retorno a estado euparatiroides luego de 6 a 36 meses post trasplante, sugiriendo involución lenta o incompleta de las glándulas paratiroides posiblemente más hiperplásicas. El retraso en nuestros pacientes es consistente en esta posibilidad. Ya que la hipercalcemia puede dañar el riñón, algunos han recomendado paratiroidectomía en todos los hipercalcémicos luego de trasplante. Por otro lado, estudios han sugerido que la hipercalcemia menor de 12 mg/dl no resulta en deterioro renal (12), lo que es consistente con la estabilidad de nuestros pacientes. La intermitencia, los valores de calcio moderadamente elevados, pero menores de 12 mg/dl no han evidenciado ningún daño en este grupo. A base de la observación radiológica normal y del análisis de contenido mineral óseo, lo bajo en un solo paciente (no publicado), no podemos inferir deterioro óseo en el grupo, indicación alterna de paratiroidectomía. Sin embargo es importante apuntar que solo histología ósea puede descartar envolvimiento esquelético.

Paratiroidectomía subtotal con auto trasplante de paratiroide es una de las formas terapéuticas de elección en aquellos pacientes que luego de un injerto renal desarrollan valores séricos de calcio mayores de 13 mg/dl, deterioro de función renal secundaria a hipercalcemia, o progreso de la osteodistrofia. Esta última indicación es aplicable a uno de nuestros 6 pacientes.

En conclusión, 6 pacientes con trasplantes funcionales se evaluaron retrospectivamente

por un período de 9 a 15 meses post trasplante. La persistencia de hipercalcemia intermitente algún tiempo post-trasplante sugiere un estado de hiperplasia paratiroidea, hiperparatiroidismo secundario e involución lenta en algunos pacientes. Con los niveles de calcio observados la ausencia de efectos secundarios tales como deterioro renal o progreso de enfermedad ósea nos permite manejo médico conservador en todos menos un paciente.

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PNEUMOCYSTIS CARINII PNEUMONIA IN A RENAL TRANSPLANT RECIPIENT: DIAGNOSIS BY TRANSBRONCHIAL BIOPSY: A CASE REPORT AND REVIEW OF THE LITERATURE

Arturo R. Córdova, MD, Orlando Vázquez MD *
José Rivera Del Río, MD and César Baldizón, MD

Abstract: A 27-year old female kidney transplant patient developed fever, cough and pulmonary infiltrates while receiving immunosuppressive therapy. A diagnosis of Pneumocystis Carinii pneumonia was made through a transbronchial lung biopsy performed at the time of fiberoptic bronchoscopy. Treatment with Trimethoprim-Sulfamethoxazole was curative. The current literature on Pneumocystis Carinii pneumonia, its diagnosis and treatment are reviewed.

Introduction

In order to diagnose Pneumocystis Carinii pneumonia the physician must have a high index of suspicion and obtain samples of bronchial secretions and/or lung tissue to confirm the presence of the organisms. This report emphasizes the usefulness of the transbronchial lung biopsy in securing tissue for the diagnosis of this disease; it is the first publi-

shed case in Puerto Rico where the diagnosis of Pneumocystis Carinii pneumonia was made using this technique. The advantages, complications and diagnostic yield of this and other diagnostic methods for this condition are reviewed.

Case Report

L. S. S. is a 27 y/o female patient who received a kidney transplant from her sister in 1975 after developing end-stage renal disease secondary to chronic glomerulonephritis diagnosed in 1973. She has developed several episodes of rejection which have been successfully treated and has remained well on Cytoxan 50 mg p.o. daily and prednisone 15 mg. p.o. daily, except for mild chronic active hepatitis and an episode of Listeria Monocytogenes Sepsis. Two months prior to admission she noticed low grade fever, arthralgias and right sternoclavicular and ankle pain. The latter were treated with Acetaminophen with improvement. She was admitted on October 20, 1979 because of persistent fever.

On physical examination, the patient had cushingoid facies and was in no acute distress. Blood pressure was 120/90, pulse 68 beats per minute and regular, respiratory rate of 18 per minute and temperature 99.0°F orally. The rest of the exam was normal except for a grade II/VI systolic ejection murmur at the left sternal border. Laboratory studies re-

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** Recipient ALA Training Grant.*



FIGURE I

vealed a hemoglobin of 12.8 g percent, a leukocyte count of 7,300 per cu mm with a differential of 90 percent Seg, 2 percent Bads, 7 percent lymphocytes and 1 percent monocytes; platelets were adequate on smear. The BUN was 29 mg percent and the serum creatinine was 2.4 mg percent. Cultures of the throat, sputum, blood and urine were negative for bacteria. Titers for cytomegalovirus and adenovirus as well as for fungi were negative. On admission, the chest X-ray and the arterial blood gases on room air were within normal limits.

She continued to have low grade fever and on October 24, 1979 developed a dry cough which worsened progressively. A chest X-ray at this time revealed a bilateral interstitial pattern predominating in the perihilar and basilar regions (Figure 1). Arterial blood gases at rest revealed a P_{O_2} of 66, a PCO_2 of 30 and a pH of 7.45. Oxygen was administered. A gallium scan revealed marked uptake in both lung fields. Physical

examination at this time was unchanged. A fiberoptic bronchoscopy was performed and transbronchial biopsies and bronchial washings were obtained and sent for appropriate studies. Except for mild bleeding of approximately 15 cc of blood, the procedure was uneventful. Grocott Silver Methenamine stains of the biopsy samples revealed multiple *Pneumocystis Carinii* organisms. (Figure 2).

Thrimethoprim-Sulfamethoxazole was administered in doses of two (2) tabs. p. o. every six hours with close monitoring of renal function.

Fever disappeared and over the ensuing two weeks the patient had become asymptomatic; significant improvement in her chest X-ray and resolution of the hypoxemia were observed. The patient was discharged home after three weeks of therapy and has shown no evidence of recurrent illness.

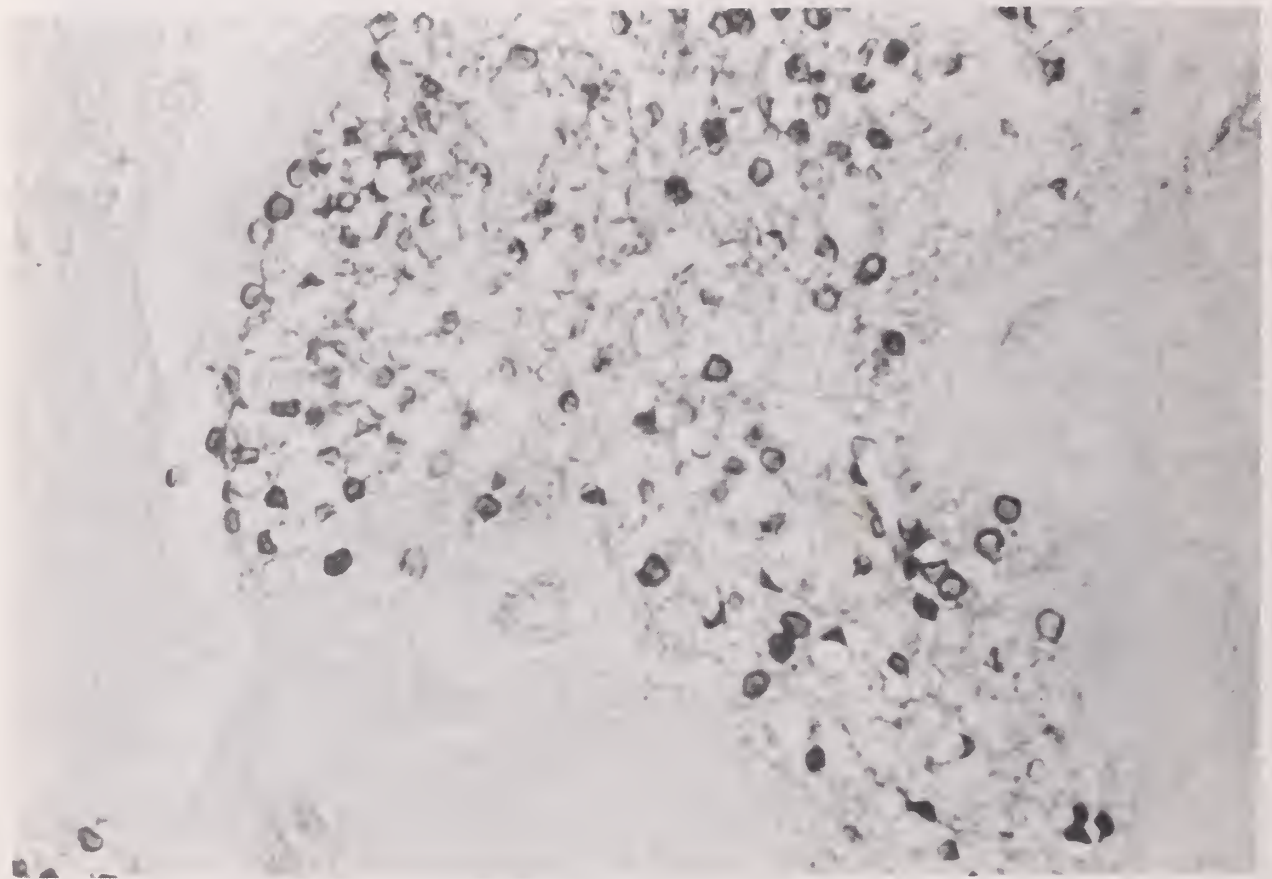


FIGURE 2

Discussion

Pneumocystis Carinii is a protozoan which characteristically causes disease in immunocompromised children and adults, although rarely it has been reported in apparently healthy persons. (1) Studies in a rat model of P. Carinii pneumonia have shown that the organism may exist in a latent form and that the development of interstitial pneumonia occurs after the administration of corticosteroids. (2) In the United States, although P. Carinii pneumonia has been reported in all age groups, the highest

incidence occurs in children less than one year old followed by children 1 to 9 years old and adults 50 to 59. (3) It occurs more frequently in patients receiving immunosuppressive or cytotoxic therapy to control acute leukemias, lymphoreticular cancers, collagen vascular diseases and transplantation rejection. (3, 4)

The clinical presentation of Pneumocystis Carinii pneumonia is non-specific. Symptoms usually include dyspnea, fever and non-productive cough without pleurisy or upper respiratory complaints; some patients may have no initial pulmonary symptoms or signs. (5) The chest

roentgenogram may show perihilar interstitial infiltrates which tend to extend peripherally, (3), localized densities (6, 7) or it may be completely normal. (5)

Laboratory values may show mild anemia, slight leukocytosis and normal platelet count. Leukopenia (leukocytes below $3,000/\text{mm}^3$) is associated with a poor prognosis. Arterial blood gases can be important specially in the subclinical early stages of the disease where hypoxemia and a respiratory alkalosis may be the only clues to pulmonary involvement. (3)

The importance of making a prompt diagnosis of *P. Carinii* pneumonia derives from the high mortality of untreated cases and the favorable response with early therapy. (3, 8) Although research is underway in the use of serologic methods for the non-invasive diagnosis of *P. Carinii* infections, presently, lack of specificity limits their value as diagnostic tools. Most cases are diagnosed by appropriate staining of lung biopsies and/or bronchial secretions'

Open lung biopsies have been used more frequently as the diagnostic method for suspected *P. Carinii* pneumonia in children and adults. This method has provided comparatively higher diagnostic yield than other biopsy techniques and allows the selection of tissue samples under direct visualization as well as insuring optimal hemostasis. (3, 9, 10) Complications are few, but in a reported series four (1.6 percent) patients died as a consequence of open lung biopsies. (3) It requires general endotracheal anesthesia and frequently logistical considerations may delay the diagnosis using this method, this may have adverse effects on patient outcome.

Several non-thoracotomy lung biopsy procedures have been used for the diagnosis of unidentified lung disease in the immunocompromised host. Percutaneous threphine lung biopsy using a pneumatic high speed drill is still advocated as a diagnostic means in some centers.

This method has a good diagnostic yield and does not require general anesthesia but requires considerable experience and skill and has a high rate of complications; pneumothorax occurs in sixty percent (60 percent) and significant hemorrhage in eighteen percent (18 percent) of cases. (11) Bleeding occurs more frequently in patients with significant azotemia.

Bronchial brush biopsy through the fiberoptic bronchoscope has been used effectively in the diagnosis of diffuse lung disease in the immunocompromised patient. (14) This technique was useful in the diagnosis of *Pneumocystis Carinii* pneumonia in 8 of 19 cases (42 percent) in the combined experience of three centers (5, 11, 15). Non bronchoscopic bronchial brushings are obtained using a flexible angiographic catheter inserted nasotracheally under fluoroscopic guidance. This method of brush biopsies has very few complications and a diagnostic yield in *Pneumocystis Carinii* pneumonia of 72 percent in two published series. (16, 17) To achieve such results nevertheless, considerable experience and sophisticated fluoroscopy equipment is necessary.

Transbronchial lung biopsies (TLB) have rapidly become an important tool in the diagnosis of diffuse pulmonary diseases during the past years. The procedure can be performed at the bedside or at the fluoroscopy suite under local anesthesia, and it can be used in patients on assisted ventilation. Preferably, it should be performed under fluoroscopic guidance but this is not indispensable. It is very well tolerated by the patient and in experienced hands, it only takes 30 to 45 minutes to perform. It has an overall diagnostic yield of 70 to 80 percent. (11, 15) It is an excellent procedure for the diagnosis of *Pneumocystis Carinii* pneumonia

where a positive diagnosis was obtained in 30 of 33 (90 percent) cases in the combined experience of several centers. (11, 15, 18, 19, 20) Pneumothorax is the most frequent complication of TLB with a frequency of 5 to 10 percent in most large series; in our experience two (2) small pneumothoraces not requiring chest tubes have occurred in a total of 33 consecutive procedures. Pneumothorax was reported in 19 percent of TLB in one series (11), but this is the exception. Bleeding is an infrequent complication of TLB in most series (11, 18, 19, 20, 21) although in a single report, bleeding of more than 100cc of blood was reported in 26 percent. (11) Fatal pulmonary hemorrhage after TLB has been reported once. (22)

Other biopsy techniques such as the percutaneous transthoracic needle aspiration biopsy have been used in the diagnosis of pulmonary diseases. Although this procedure has excellent yield in the diagnosis of localized peripheral pulmonary disease, (23) in general, in the adult, it is less effective in diagnosing diffuse lung disease when compared to TLB. Overall, the risk of pneumothorax is about twenty percent (20 percent) with mild bleeding occurring in five percent (5 percent). (24) A high frequency of bleeding has been reported with this procedure in a series of immunocompromised patients. (26)

Bronchial washings (BW) are usually less effective than TLB or brushings in the diagnosis of diffuse lung disease. Some authors report considerable success in the microbiologic diagnosis of infection in the compromised host using this technique, (14) but the results are difficult to interpret due to the frequent contamination of bronchoscopically obtained washings with upper airway secretions. (26) Reports have recently shown excellent yield in the diagnosis of *Pneumocystis Carinii* pneumonia using subsegmental bronchial washings. (19, 27)

Due to the peripheral location of the pathologic lesion in *Pneumocystis Carinii* pneumonia, the demonstration of the organism in sputum or suctioned tracheal samples has been infrequent (3, 29), but due to the relative ease with which these samples can be obtained, they should always be considered in the evaluation of these patients.

Appropriate staining techniques are crucial to optimize the yield of the diagnostic procedures. Grocott and Gomori silver methenamine stains are the most reliable methods of staining (30), although other methods have been used successfully by some authors. (9) Touch preparations from lung biopsy specimens should be made on glass slides and sent for silver impregnation stains; this approach takes three hours to process while the preparation of stained histologic sections may take several days.

Until recently, Pentamidine isethionate has been the treatment of choice for *Pneumocystis Carinii* pneumonia. Although effective if begun early in the course of the disease, adverse reactions occur in close to 50 percent of the cases. Azotemia occurs in 25 percent of those treated and is the most frequent side effect, followed by abnormal liver function tests in 10 percent, hypoglycemia in 6 percent, hematologic disturbances in 4 percent and skin rashes and hypocalcemia in approximately 1 percent each. (3) Due to the high rate of toxic reactions, empirical treatment with Trimethoprim, 20 mg/kg and Sulfamethoxazole 100 mg/kg (TMP-SMZ) was tried in children with *Pneumocystis*. A controlled randomized study comparing Pentamidine and TMP-SMZ revealed that both treatments were equally effective and that some patients which failed to respond to one drug responded to the other and vice-versa. (8) Similar results have been reported in adults and despite the use of doses three to four times larger than those recommended for urinary tract infec-

tions, no serious untoward reactions have occurred. (32) Trimethoprim is a potent inhibitor of microbial dihydrofolate reductase, the enzyme responsible for the reduction of dihydrofolate to tetrahydrofolate. Since it binds to mammalian dihydrofolate reductase 50,000 times less than to the bacterial enzyme, a wide margin of safety should exist with human usage. (32) Despite of this, thrombocytopenia and leukopenia have been reported in a patient with bone marrow transplantation due to aplastic anemia. This resolved with discontinuation of the drug and the administration of folinic acid. (31) TMP and ZMZ serum level determinations are desirable whenever possible in view of the wide range of serum levels obtained due to variations in the absorption of the drugs from the G. I. tract. Poor excretion in patients with azotemia can result in high serum levels. Low levels are usually caused by inadequate oral absorption due to ileus; these cases should receive intravenous TMP-SMZ. The role of TMP-SMZ in the long term chemoprophylaxis against *Pneumocystis Carinii* infections in populations at risk is being evaluated prospectively. (33)

Immunosuppressed patients, including transplant recipients, are always at risk to develop infectious pulmonary complications. Indeed, infection is the number one cause of death in these patients. Constant monitoring is needed to detect and manage complications as early as possible. A protocol-guided, aggressive policy for early diagnosis using the methods described, is the only way to improve prognosis. (34)

Conclusions

Pneumocystis Carinii pneumonia should be suspected in immunocompromised hosts presenting with impaired gas exchange regard-

less of whether symptoms or interstitial infiltrates are present on chest radiograph. A transbronchial lung biopsy through a fiberoptic bronchoscope is a safe and efficient means for the prompt diagnosis of this condition. Concomitant bronchial brushings and segmental bronchial washings maximize the diagnostic yield. This combination is the procedure of choice for the diagnosis of suspected *Pneumocystis Carinii* pneumonia. In patients with severe azotemia, with uncontrollable clotting abnormalities or severe pulmonary hypertension, only the bronchial brushings and washings should be done because of the high risk of bleeding.

The treatment of choice is Trimethoprim-Sulfamethoxazole but Pentamidine Isethionate should be considered in confirmed cases who do not respond.

An aggressive diagnostic policy is the only way to prevent the otherwise disastrous course of pulmonary infectious complications in immunosuppressed hosts.

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†See Warnings, Precautions and Adverse Reactions.

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Final classification of the less-than-effective indications requires further investigation.

CONTRAINDICATIONS: Obstructive uropathy (for example, bladder neck obstruction due to prostatic hypertrophy); obstructive disease of the gastrointestinal tract (as in achalasia, pyloroduodenal stenosis); paralytic ileus, intestinal atony of the elderly or debilitated patient, unstable cardiovascular status in acute hemorrhage; severe ulcerative colitis; toxic megacolon complicating ulcerative colitis; myasthenia gravis. **WARNINGS:** In the presence of a high environmental temperature, heat prostration can occur with drug use (fever and heat stroke due to decreased sweating). Diarrhea may be an early symptom of incomplete intestinal obstruction, especially in patients with ileostomy or colostomy. In this instance treatment with this drug would be inappropriate and possibly harmful. Bentyl may produce drowsiness or blurred vision. In this event, the patient should be warned not to engage in activities requiring mental alertness such as operating a motor vehicle or other machinery or perform hazardous work while taking this drug. **PRECAUTIONS:** Although studies have failed to demonstrate adverse effects of dicyclomine hydrochloride in glaucoma or in patients with prostatic hypertrophy, it should be prescribed with caution in patients known to have or suspected of having glaucoma or prostatic hypertrophy. Use with caution in patients with Autonomic neuropathy. Hepatic or renal disease. Ulcerative colitis. Large doses may suppress intestinal motility to the point of producing a paralytic ileus and the use of this drug may precipitate or aggravate the serious complication of toxic megacolon. Hyperthyroidism, coronary heart disease, congestive heart failure, cardiac arrhythmias, and hypertension. Hiatal hernia associated with reflux esophagitis since anticholinergic drugs may aggravate this condition.

Do not rely on the use of the drug in the presence of complication of biliary tract disease. Investigate any tachycardia before giving anticholinergic (atropine-like) drugs since they may increase the heart rate. With overdosage, a curare-like action may occur. **ADVERSE REACTIONS:** Anticholinergics/antispasmodics produce certain effects which may be physiologic or toxic depending upon the individual patient's response. The physician must delineate these. Adverse reactions may include xerostomia; urinary hesitancy and retention; blurred vision and tachycardia; palpitations; mydriasis; cycloplegia; increased ocular tension; loss of taste; headache; nervousness; drowsiness; weakness; dizziness; insomnia; nausea; vomiting; impotence; suppression of lactation; constipation; bloated feeling; severe allergic reaction or drug idiosyncrasies including anaphylaxis; urticaria and other dermal manifestations; some degree of mental confusion and/or excitement, especially in elderly persons; and decreased sweating. With the injectable form there may be a temporary sensation of lightheadedness and occasionally local irritation. **DOSE AND ADMINISTRATION:** Dosage must be adjusted to individual patient's needs.

Usual Dosage: Bentyl 10 mg. capsule and syrup: Adults: 1 or 2 capsules or teaspoonfuls syrup three or four times daily. Children: 1 capsule or teaspoonful syrup three or four times daily. Infants: ½ teaspoonful syrup three or four times daily (May be diluted with equal volume of water.) Bentyl 20 mg.: Adults: 1 tablet three or four times daily. Bentyl Injection: Adults: 2 ml. (20 mg.) every four to six hours intramuscularly only. NOT FOR INTRAVENOUS USE. **MANAGEMENT OF OVERDOSE:** The signs and symptoms of overdose are headache, nausea, vomiting, blurred vision, dilated pupils, hot, dry skin, dizziness, dryness of the mouth, difficulty in swallowing, CNS stimulation. Treatment should consist of gastric lavage, emetics, and activated charcoal. Barbiturates may be used either orally or intramuscularly for sedation but they should not be used if Bentyl with Phenobarbital has been ingested. If indicated, parenteral cholinergic agents such as Urecholine[®] (bethanechol chloride USP) should be used.

Product Information as of October, 1978.

Injectable dosage forms manufactured by CONNAUGHT LABORATORIES, INC., Swiftwater, Pennsylvania 18370 or TAYLOR PHARMACAL COMPANY, Decatur, Illinois 62525 for MERRELL-NATIONAL LABORATORIES, Division of Richardson-Merrell Inc., Cincinnati, Ohio 45215, U.S.A.

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AVAILABLE ONLY ON PRESCRIPTION

Brief Summary

INDICATIONS: For the prevention and treatment of nocturnal recumbency leg muscle cramps, including those associated with arthritis, diabetes, varicose veins, thrombophlebitis, arteriosclerosis, and static foot deformities.

CONTRAINDICATIONS: Because of the quinine content, Quinamm is contraindicated in women of childbearing potential, in pregnancy, in patients with known quinine sensitivity, and in patients with glucose-6-phosphate dehydrogenase deficiency. Hemolysis (with the potential for hemolytic anemia) has been associated with a G-6-PD deficiency in patients taking quinine.

PRECAUTIONS: Thrombocytopenic purpura may follow the administration of quinine in highly sensitive patients. Recovery will follow withdrawal of the medication.

Cinchona alkaloids, including quinine, have the potential to depress the hepatic enzyme system that synthesizes the vitamin K-dependent factors. The resulting hypoprothrombinemic effect may enhance the action of warfarin and other oral anticoagulants.

ADVERSE REACTIONS: Aminophylline may produce intestinal cramps in some instances, and quinine may produce symptoms of cinchonism, such as tinnitus, dizziness, and gastrointestinal disturbance. If ringing in the ears, deafness, skin rash, or visual disturbances occur, the drug should be discontinued.

DOSE AND ADMINISTRATION:

1 tablet upon retiring. When necessary, 1 additional tablet may be taken following the evening meal.

Product Information as of September, 1977

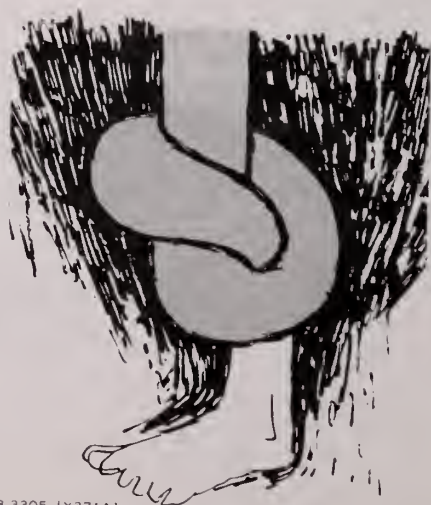
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* Central alpha-adrenergic stimulation decreases sympathetic outflow from the brain, as shown in animal studies.

¹ Data on file at Boehringer Ingelheim Ltd.

Please see last page for brief summary, including warnings, precautions, and adverse reactions.

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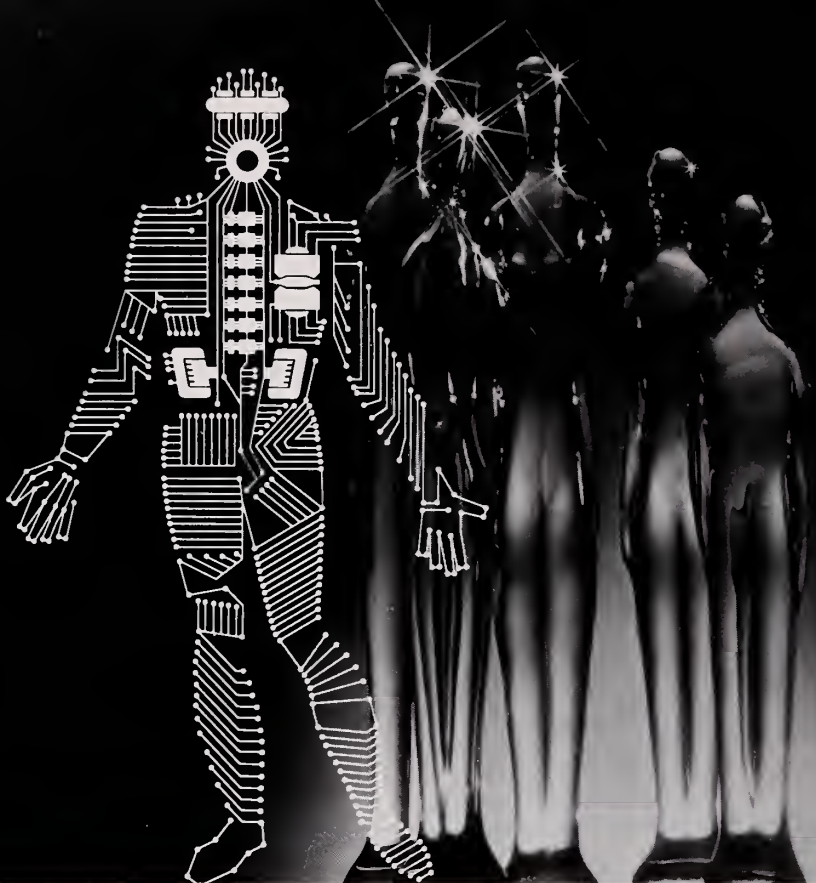
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Hypertension



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Hypertension



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- Effective in all degrees of hypertension. It is mild to moderate in potency.
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Indication: The drug is indicated in the treatment of hypertension. As an anti-hypertensive drug, Catapres (clonidine hydrochloride) is mild to moderate in potency. It may be employed in a general treatment program with a diuretic and/or other antihypertensive agents as needed for proper patient response.

Warnings: Tolerance may develop in some patients necessitating a reevaluation of therapy.

Usage in Pregnancy: In view of embryotoxic findings in animals, and since information on possible adverse effects in pregnant women is limited to uncontrolled clinical data, the drug is not recommended in women who are or may become pregnant unless the potential benefits outweigh the potential risk to mother and fetus.

Usage in Children: No clinical experience is available with the use of Catapres (clonidine hydrochloride) in children.

Precautions: When discontinuing Catapres (clonidine hydrochloride), reduce the dose gradually over 2 to 4 days to avoid a possible rapid rise in blood pressure and associated subjective symptoms such as nervousness, agitation, and headache. Patients should be instructed not to discontinue therapy without consulting their physician. Rare instances of hypertensive encephalopathy and death have been recorded after cessation of clonidine hydrochloride therapy. A causal relationship has not been established in these cases. It has been demonstrated that an excessive rise in blood pressure, should it occur, can be reversed by resumption of clonidine hydrochloride therapy or by intravenous phentolamine. Patients who engage in potentially hazardous activities, such as operating machinery or driving, should be advised of the sedative effect. This drug may enhance the CNS-depressive effects of alcohol, barbiturates and other sedatives. Like any other agent lowering blood pressure, clonidine hydrochloride should be used with caution in patients with severe coronary insufficiency, recent myocardial infarction, cerebrovascular disease or chronic renal failure.

As an integral part of their overall long-term care, patients treated with Catapres (clonidine hydrochloride) should receive periodic eye examinations. While, except for some dryness of the eyes, no drug-related abnormal ophthalmologic findings have been recorded with Catapres (clonidine hydrochloride), in several studies the drug produced a dose-dependent increase in the incidence and severity of

The usual starting dose of Catapres is 0.1 mg at breakfast and 0.1 mg at bedtime. Some patients may benefit from a starting dose of 0.1 mg at bedtime.

Usual daily dose range—0.2—0.8 mg

Maximum daily dose—2.4 mg

Doses as high as this have rarely been employed.

For optimal results, the dose of Catapres must be adjusted according to the patient's individual blood pressure response.

spontaneously occurring retinal degeneration in albino rats treated for 6 months or longer.

Adverse Reactions: The most common reactions are dry mouth, drowsiness and sedation. Constipation, dizziness, headache, and fatigue have been reported. Generally these effects tend to diminish with continued therapy. The following reactions have been associated with the drug, some of them rarely. (In some instances an exact causal relationship has not been established.) These include: Anorexia, malaise, nausea, vomiting, parotid pain, mild transient abnormalities in liver function tests; one report of possible drug-induced hepatitis without icterus and hyperbilirubinemia in a patient receiving clonidine hydrochloride, chloralhydrate and papaverine hydrochloride. Weight gain, transient elevation of blood glucose, or serum creatine phosphokinase: congestive heart failure, Raynaud's phenomenon; vivid dreams or nightmares, insomnia, other behavioral changes, nervousness, restlessness, anxiety and mental depression. Also rash, angioneurotic edema, hives, urticaria, thinning of the hair, pruritus not associated with a rash, impotence, urinary retention, increased sensitivity to alcohol, dryness, itching or burning of the eyes, dryness of the nasal mucosa, pallor, gynecomastia, weakly positive Coombs' test, asymptomatic electrocardiographic abnormalities manifested as Wenckebach period or ventricular trigeminy.

Overdosage: Profound hypotension, weakness, somnolence, diminished or absent reflexes and vomiting followed the accidental ingestion of Catapres (clonidine hydrochloride) by several children from 19 months to 5 years of age. Gastric lavage and administration of an analeptic and vasopressor led to complete recovery within 24 hours. Tolazoline in intravenous doses of 10 mg at 30-minute intervals usually abolishes all effects of Catapres, (clonidine hydrochloride) overdosage.

How Supplied: Catapres, brand of clonidine hydrochloride, is available as 0.1 mg (tan) and 0.2 mg (orange) oval, single-scored tablets in bottles of 100 and 1000. Also available as 0.3 mg (peach) oval, single-scored tablets in bottles of 100.

For complete details, please see full prescribing information.

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PREGNANCY FOLLOWING RENAL TRANSPLANTATION

Robert W. Axtmayer, MD, FACOG

Pregnancy is not without risk following renal transplantation. Both fetus and mother share this risk and therefore some observers have advised that sterilization be offered at the time of transplantation. Certain methods of contraception may be contraindicated in the transplant patient. As they are immunosuppressed there is risk of infection if an intrauterine device were to be inserted. The use of oral contraceptives is also to be avoided as hypertension is more frequent in these patients. Barrier methods of contraception seem to be better suited. It is advisable that before undergoing a pregnancy, creatinine values should be less than 2 mg/100ml, and there should be no hypertension or proteinuria. Ideally, I.V.P. should show normal renal pelvis and calyces and the dose of prednisone should be under 13 mg/day and that of azathioprene 3 mg/kg/day or less. (1)

To achieve pregnancy may be difficult for the transplant patient. Usually the patient with chronic renal insufficiency is anovulatory and amenorrheic. This may be due to a decrease in circulating gonadotropin. These patients usually improve if transplan-

tation is successful and menstrual and ovarian function may then become normal. It is advisable that conception be delayed for one to two years following transplantation. Some investigators have reported these pregnancies not to be entirely uncomplicated as malformed fetuses appear to be more frequent probably as a result of immunosuppression. Also, hypertension, dystosis due to the abnormally placed kidney, hyperglycemia, uterine rupture and maternal death have been reported. Death following transplantation may be due to renal rejection, sepsis, gastrointestinal hemorrhage, myocardial infarction, cerebral vascular accident, or pulmonary embolus. (2, 3). A 24-year old patient who became pregnant after receiving a kidney transplant is presented. Special emphasis is made on her medical and obstetrical case.

Case Report

Patient L. C. R. was born in St. Vincent's Hospital, New York, on Oct. 11, 1956. She was born at term being the third child in the family. Birth weight was over 8 lbs. The mother reported the external genitalis of the infant as "abnormal". There was a doubt as to whether she had received "hormones" during pregnancy. In any event the infant had an enlarged clitoris but 17-Ketosteroid excretion was normal. There were also several urinary tract ano-

From the San Juan Municipal Hospital, Department of Obstetrics and Gynecology, Río Piedras, P. R.

malies which consisted of: "bilateral hydronephrosis with a urogenital sinus". Her early years were marked by recurrent urinary tract infections. There were several admissions to the hospital. During 1963 a clitoridectomy was performed. There were bouts of urinary retention. Voiding cystogram on Oct. 17, 1966 showed a "huge" bladder with evidence of right vesicourethral reflux extending to the level of the right iliac crest. On June 3, 1969 there was poor delineation of both renal shadows. Films suggested marked renal impairment, worse on the left side probably due to "chronic inflammatory changes". She was 13 years old at the time. Urologic cystoscopic exam showed a common opening for urethra and vagina but the ureters could not be visualized. The cervix could not be seen and the uterus was not felt at that time. The introitus was very small. Patient had had menarche at 11 years of age. The periods were every 30 days, lasting for 4 days with moderate bleeding. Her renal function progressively deteriorated. On July 10, 1972, creatinine clearance was over 3.0 m percent. From 1973 on she was not seen by us until 4 Oct. 1978 when she was admitted to our service. At that time she gave a history of having had renal transplant operation at Tucson VA Hospital on 29 Jan. 1976 and later followed at the San Juan VA Hospital. Her LMP had been on 20 March 1977 and her EDC was for 27 Dec. 1978. She was on Imuran 50 mg daily; Prednisone 25 mg, q.o.d.; and Lasix 40 mg. daily. She had also received sulfisoxazole for a recent urinary tract infection. The serum creatinine was 0.8 mg/dl.; the BUN was 13.0 mg/dl. Hgb was 11.0 g/dl. The creatinine clearance was 49 ml/min. She was discharged and readmitted on 5 Nov. 1978 because of uterine contractions. Serum creatinine was 0.8 mg/dl and Bun 15 mg/dl. Creatinine clearance was 54 ml/min. Urine cultures did not show any growth. Sonographic evaluation on 13 Nov. 1978 showed the biparietal diameter (BPD) at 8.0 cm corresponding to a fetal age of 33 weeks. When compared to a sonogram of 9 Oct. 1978 this showed growth of 1.0 cm in the BPD. Dilatation of the transplanted ureter was evident. On 30 Nov. 1978 repeat ultrasonographic exam showed a BPD of 8.2 cm. corresponding with a gestational age of 33.6 weeks. The BP was 120/80. The uterine fundus was 4 finger breadths below the xiphoid and a mass was felt in

the RLQ which was thought to represent the transplanted kidney. The fetal heart was heard in the RLQ at 140 beats per minute. Pelvic exam showed a very narrow introitus. The cervix was closed. Renal dynamic studies done at San Juan VA Hospital showed mild ureterohydronephrosis without marked delay in passage to the bladder of contrast material. Daily monitoring of BP, fetal heart, were done. On 8 Dec. 1978, at 37 weeks gestation her creatinine clearance was 35.1 ml/min., BUN 12 mg percent, and creatinine 0.8 mg percent. On 11 Dec 1978 amniocentesis was done under sonographic visualization. The BPD was 8.8 cm. which correlated with 36.5 weeks gestation. Amniotic fluid studies showed L/S Ratio of 5.7, creatinine of 2.6 mg/dl, bilirubin of 0.2 mg/dl and OD of 0.380. On Dec. 14, 1978 a classical cesarean section was done. A term male baby in breech presentation was delivered with an Apgar score of 7. The weight was 5 lbs. 3 oz. A bicornuate uterus was found with the pregnancy in the left horn. The right horn was enlarged to about 12 cm. The transplanted kidney appeared to be of normal size. Blood loss was estimated at 700 cc. Pomeroy sterilization was carried out. Postoperatively she was kept on Imuran and prednisone. There were no complications. She was discharged on Dec. 28, 1978. The baby also did well and was discharged in good condition. The patient has continued to do well after operation and was last seen at the VA Hospital on December 1979 with normal renal function. No evidence of malformation on the baby has been observed.

Comments

During pregnancy many changes take place in the urinary tract. There is dilatation, and diminution in peristalsis; GFR (glomerular filtration rate) increases 30 to 50 percent. Values of urea nitrogen and serum creatinine decrease to around 13 mg/100 ml. and 0.8 mg/100 ml. in the normal pregnant woman.

The number of reported pregnancies in the renal transplant patient is steadily increasing. Up to 1975 there were less than 100 preg-

nancies in women who had transplants. Surely, more of these patients will in the future be in need of medical attention during pregnancy. Although the woman who receives her kidney from a living related donor has more success with her pregnancy than one who has received a cadaver kidney, the latter may also succeed. As reported by Makowski and Penn (3) in 35 pregnancies in 25 gravidas, they found spontaneous abortion, and hypertension to be among the more frequent complications. They reported 25 percent hypertension in those patients whose B. P. was normal before pregnancy and worsening of B. P. in three patients who were hypertensive before gestation. They reported 22 live births in 35 pregnancies of which 9 infants were entirely normal. The most frequent complications in the newborns were: prematurity (10) respiratory distress syndrome (4) congenital anomalies (3) hypoadrenalism (2) and neonatal septicemia (2).

For the mother, many complications may affect her well-being. The more common are: toxemia, hypercalcemia, and because of the ingestion of immunosuppressants, bacterial, viral and fungal infections. Also urinary tract infections, *Candida albicans* infection, hepatitis, sinusitis and others have been reported. When membranes rupture prematurely management must be aggressive and pelvic examinations must be done under aseptic conditions and kept to a minimum. During pregnancy, renal function is monitored by measuring blood urea nitrogen and serum creatinine, levels of 18-28 mg/100 ml. and 0.18-2.0 mg/100 ml. respectively being in the

accepted tolerable range. In around 40 percent of patients there may be deterioration of function while in 60 percent creatinine clearance increased. (4) Estriol determinations in the patient who is receiving corticoids are not of value in assessing fetal well-being as the maternal administration of glucocorticoids suppresses fetal adrenal precursors giving false low values. It is not clear whether human placental lactogen measurement may substitute estriol determinations as placental lactogen is a measurement of syncytiotrophoblast and following these levels may not correlate well with fetal well-being. Creatinine determinations in the amniotic fluid are high if the mother has an elevated serum creatinine and are of no value in estimating fetal maturity.

The need for terminating pregnancy by Cesarean Section may arise. Actually, the transplanted kidney rarely causes dystocia as it is placed in the false pelvis. One must be on the lookout for both fetal and maternal indications for Cesarean Section in this group of patients.

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LA REHABILITACION EN EL PACIENTE TRASPLANTADO

David Matos Alvarado, Norma Rodríguez-Palmer
Rosa Ivette Santiago Román, María del Carmen Torres Ramos
y Ana María Zayas de Jesús

Este estudio fue llevado a cabo por un grupo de estudiantes de la Escuela Graduada de Consejería en Rehabilitación, de la Universidad de Puerto Rico en el año 1977 al 78. El propósito del mismo fue el identificar el grado de rehabilitación del paciente trasplantado. (1) Sobre este tema no se había hecho hasta el momento estudio alguno en Puerto Rico. El estudio se llevó a cabo en el Hospital de Veteranos de San Juan, Puerto Rico, con la colaboración de los miembros del Programa de Transplante de Puerto Rico. (2)

Las observaciones que llevaron a este estudio eran las siguientes: El trasplante de riñón cura un gran número de pacientes con fallo renal; se dice además que "mejora la calidad de la vida". Examinando críticamente estas premisas, nos preguntamos los autores:

- (1) ¿De veras se rehabilita el paciente que recibe un trasplante?
- (2) ¿Permite el trasplante renal devolver al paciente a una vida normal, productiva, feliz y de bienestar, o es solo una prolongación artificial de una vida enferma?

Siendo este tema de tanto interés para los autores y de tanta relevancia para los sistemas de prestación de salud en el país, formulamos entonces los siguientes objetivos:

- (1) Determinar el grado de rehabilitación del paciente trasplantado en sus distintas esferas funcionales:
 - (a) *Empleo:* ¿Se reintegra a su trabajo? ¿Ruelve a una vida productiva?
 - (b) *Familia:* ¿Es aceptado como persona normal o se le da trato especial por su condición? ¿Lleva a cabo su rol de jefe, esposo, padre, hijo, etc.?
 - (c) *Interacción Social:* ¿Comparte con su mundo social de una manera normal, o como lo solía hacer antes?
 - (d) *Recreación:* ¿Lleva una vida normal como lo hacía antes de su enfermedad? ¿Se recrea con sus amigos, deportes, actividades?
 - (e) *Sexo:* ¿Lleva una vida sexual normal con su pareja?

De la Escuela Graduada de Consejería en Rehabilitación,
Universidad de Puerto Rico

(2) Determinar cuáles son los factores que intervienen en su rehabilitación, bien sea ayudando u obstaculizando la misma:

(a) Nivel educacional y económico.

(b) Aspectos de su enfermedad, de los medicamentos, operación, drogas, complicaciones, miedo al rechazo, etc.

(c) Aspectos familiares.

(d) Aspectos sociales

(e) Religión.

(f) Aspectos sicosociales, incluyendo personalidad, amigos y otras influencias, preocupaciones.

(3) Determinar el impacto económico en el presupuesto familiar antes y después del trasplante.

(4) Determinar si existe la necesidad de servicios de consejería en rehabilitación en un Programa de Trasplantes.

Modelo Experimental

Definiciones Operacionales: Entendemos que algunas definiciones están en orden:

1. *Factores sico-sociales:* Elementos internos y externos (amigos, preocupaciones, personalidad) que afectan la rehabilitación del paciente de trasplante renal.

2. *Factores socio-económicos:* Es aquel conjunto de variables peculiares de orden social y económico (educación, empleo, etc.) que caracteriza en términos generales al paciente de trasplante renal y que al mismo tiempo los señalan y representan como grupo.

3. *Grado de Rehabilitación:* Hasta qué punto el paciente de trasplante renal se rehabilita en las distintas esferas funcionales. Los autores consideran que el sujeto trasplantado con 75 por ciento o más de grado de rehabilitación está rehabilitado.

4. *Reacción Positiva:* Actividades familiares que ayudan al paciente de trasplante renal en el proceso de rehabilitación.

5. *Vida Plena y Normal:* Conjunto de actividades y funciones que el paciente de trasplante renal realiza en una forma autosuficiente luego de ser trasplantado (actividades tales como: trabajo, organizaciones cívicas, campañas para ayudar a la comunidad, deportes, actividades recreativas).

Se utilizó para este experimento un cuestionario elaborado por los autores en combinación con los miembros del Programa de Trasplante. Consistía de 38 preguntas generales, cada cual con distintas secciones y acápites. El paciente era entrevistado por dos de los autores después de haber desarrollado cierto grado de familiaridad y amistad con el mismo. Las preguntas eran pesadas para efectos del análisis.

El diseño utilizado en este estudio fue diagnóstico descriptivo en un tiempo y con una celda. La muestra consistió de 18 pacientes, de los cuales 12 eran varones y 6 mujeres, entre las edades de 15 a 50 años.

Una vez establecido los criterios de evaluación, se analizó cada pregunta como positiva o negativa. Se estableció que el sujeto trasplantado con un 75 por ciento o más de grado de rehabilitación estaba rehabilitado para efectos de nuestro estudio. Se le dio más importancia a las siguientes esferas funcionales: familia, empleo, amigos, cónyuge, bienestar físico, auto imagen y sexo; estas variables analizadas antes del trasplante, durante el fallo renal, y después del trasplante.

Resultados

De los 18 pacientes trasplantados, un 66 por ciento cayeron en la categoría de totalmente rehabilitados y un 34 por ciento demostraron una rehabilitación parcial. Este 34 por ciento estaba, para nuestros efectos

rehabilitados, pero no habían sido reestablecidos a su trabajo, de manera que no caían bajo rehabilitación total. Aun estos pacientes parcialmente rehabilitados demostraban tener un gran potencial de rehabilitación, i.e., más de un 50 por ciento de las preguntas contestadas en sentido positivo.

Los factores que se tomaron en consideración en la rehabilitación de los sujetos demostraron lo siguiente:

- (1) Una reacción positiva de parte de la familia hacia el paciente trasplantado aparentaba ser lo más importante en su rehabilitación. Esto se vio casi en la totalidad de aquellos pacientes que tenían rehabilitación total.
- (2) El ser proveedor en el hogar estimula grandemente a estos sujetos ya que se sienten en la necesidad moral de buscar una rehabilitación rápida.

	<i>Previo</i>	<i>Durante el Fallo Renal</i>	<i>Después del Trasplante</i>
<i>Familia</i>	<i>N</i>	↓	↑ <i>N</i>
<i>Empleo</i>	<i>N</i>	↓↓	↑
<i>Amigos y Social</i>	<i>N</i>	±	<i>N</i>
<i>Cónyuge</i>	<i>N</i> ±	↓↓	↑± <i>N</i>
<i>Bienestar</i>	<i>N</i>	↓↓	↑± <i>N</i>
<i>Auto-Imagen</i>	<i>N</i>	↓↓	↑± <i>N</i>
<i>Sexo</i>	<i>N</i>	↓↓	↑± <i>N</i>

- (3) Los factores de sexo, edad, y escolaridad, para sorpresa nuestra, no jugaban papel alguno en si el paciente iba a tener una rehabilitación rápida o total.
- (4) La religiosidad, a pesar de ser considerado por los distintos pacientes como un factor importante, no se pudo juzgar estadísticamente ya que la mayoría de ellos eran religiosos. De la misma manera, una de las personas rehabilitadas completamente no ostentaba credo religioso alguno.

Conclusiones

De este estudio, los autores concluyen que la mayoría de los pacientes trasplantados se rehabilitan; (3, 4) que la mayoría de estos pacientes retornan a una vida productiva; que la calidad de la vida del paciente mejora grande y significativamente y que se puede decir que se les devuelve a la mayoría a una vida plena

y casi normal; y por último, que lo más importante en la rehabilitación del paciente es que mantenga una interacción positiva con su familia.

Agradecimiento

Los autores agradecen la cooperación de los pacientes trasplantados, y del personal del Programa de Trasplantes de Puerto Rico, Hospital de Veteranos.

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3. Miller, G. M.: Moral and Ethical Implications of Human Organ Transplants, Illinois, Springfield, Charles C. Tomas, 1971.
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M E D I – Q U I Z

1. En Puerto Rico la incidencia de enfermedad renal terminal es:
 - a. Inexistente
 - b. 75-100 casos nuevos/millón/año
 - c. 500 casos nuevos/millón/año
2. El tratamiento de enfermedad renal terminal con diálisis y trasplante es costoso. En Puerto Rico:
 - a. El paciente lo paga todo
 - b. El Gobierno Estatal lo paga todo
 - c. El Gobierno Federal (Medicare) paga 80 por ciento de los costos de diálisis y 100 por ciento de los costos de trasplante
3. En Puerto Rico existen los siguientes programas:
 - a. Diálisis de hospital
 - b. Diálisis en el hogar
 - c. Diálisis de cuido mínimo
 - d. Trasplante de riñón
 - e. Diálisis y trasplante en niños
 - f. Todos
 - g. a y d sólo
4. Contraindicación absoluta para trasplante es (son):
 - a. Sepsis
 - b. Edad

- c. Cáncer Sistémico
 - d. Vejiga dañada
 - e. Lupus
 - f. Todas
 - g. Ninguna
 - h. a y c solo
5. Los resultados de trasplante de riñón en vejigas artificiales son:
- a. Iguales
 - b. Peores
 - c. Mejores
- que en la vejiga normal.
6. Los antígenos de histocompatibilidad de los puertorriqueños:
- a. Reflejan influencia negra, indígena y europea
 - b. Su proporción es diferente a otras poblaciones
 - c. Predice mejores resultados con órganos locales que importados
 - d. Todas
 - e. a y c
7. En trasplante se ve mayor incidencia que en la población normal, de:
- a. Tumores
 - b. Fracturas patológicas
 - c. Infección con organismos intracelulares

- d. Sicosis
 - e. a, b, c
 - f. Todos
8. En Puerto Rico:
- a. Sobreviven 90 por ciento de los pacientes y 80 por ciento de los riñones trasplantados de donante vivo
 - b. Se rehabilitan parcialmente 100 por ciento, y totalmente (trabajo o estudio) 66 por ciento de los pacientes trasplantados
 - c. Las complicaciones observadas en donantes vivos son más bajas que en los Estados Unidos
 - d. Existe una ley para facilitar la donación para trasplantes
 - e. Todas
 - f. a y b solamente
9. La mejor manera de diagnosticar rechazo incluye:
- a. Renograma
 - b. Arteriograma
 - c. Creatinina
 - d. Aumento en la reactividad de los linfocitos
 - e. Todos
 - f. a y c
10. Embarazo para la paciente trasplantada:
- a. Está prohibido
 - b. Traumatiza el riñón durante el parto
 - c. Aumenta la incidencia de bebés de bajo peso
 - d. Causa distocia por el riñón pélvico.

When a problem feeder cries... **COULD IT BE MORE THAN JUST THE MILK?**

There are many reasons for infant feeding problems, and it's not always easy to determine the source.

Frequent causes of infant feeding problems are an intolerance to cow's milk or corn.

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1. Committee on Nutrition: Commentary on breast feeding and infant formulas, including proposed standards for formulas. Ped 52:278-285, 1976.

In recurrent urinary tract infections



Septra[®] DS

Each tablet contains:
160 mg trimethoprim and 800 mg sulfamethoxazole

B.I.D.

**where
the action is.**

In the kidney

Septra DS provides effective antibacterial action in the kidneys, via urine and blood, against susceptible strains of E coli, Klebsiella-Enterobacter, Proteus mirabilis, Proteus vulgaris and Proteus morganii.

The high degree of efficacy of Septra DS was confirmed in a study of 59 patients with recurrent pyelonephritis. All patients had upper urinary tract disease as evidenced by fever $\geq 100.4^{\circ}$ F and/or flank pain, and $\geq 10^5$ organisms/ml of urine. After two weeks' therapy and up to seven days post-therapy, Septra achieved bacteriologic cure ($\leq 10,000$ organisms/ml of urine) in 91.5% of patients.¹

And during the critical "recurrence" period from one to four weeks post-therapy, this excellent response rate was well maintained. Of the 53 patients evaluated at that time, 51 (96.2%) were still infection free.¹

Unlike many other antibacterials for the treatment of urinary tract infections, Septra DS is administered on a convenient b.i.d. dosage schedule.

In the bladder

What makes Septra DS good for the tough areas—the kidneys—makes it good for the not-so-tough. Septra DS provides antibacterial action in the bladder, via urine and blood, against susceptible strains of major pathogens that cause recurrent cystitis.



And along the route to recurrence

During therapy, Septra DS diffuses into vaginal fluid² and into the bowel.^{3,4} By eliminating potential uropathogens from the fecal flora, and bathing the periurethral area in an "antibacterial" vaginal fluid, Septra DS helps block the most common route to reinfection in women.

Maintain adequate fluid intake and perform frequent urinalyses with careful microscopic examination during therapy. Septra is contraindicated in children under two months old.

Please see prescribing information on next page.



Burroughs Wellcome Co.
Research Triangle Park
North Carolina 27709

Septra® DS B.I.D.

Each tablet contains: 160 mg trimethoprim and 800 mg sulfamethoxazole

Septra® Suspension B.I.D.

Each teaspoonful (5 ml) contains: 40 mg trimethoprim and 200 mg sulfamethoxazole

Septra® DS Tablets Double Strength

Septra® Tablets

Septra® Suspension

INDICATIONS AND USAGE:

URINARY TRACT INFECTIONS: For the treatment of urinary tract infections due to susceptible strains of the following organisms: *Escherichia coli*, *Klebsiella-Enterobacter*, *Proteus mirabilis*, *Proteus vulgaris*, *Proteus morganii*. It is recommended that initial episodes of uncomplicated urinary tract infections be treated with a single effective antibacterial agent rather than the combination.

NOTE: Currently, the increasing frequency of resistant organisms is a limitation of the usefulness of all antibacterial agents, especially in the treatment of these urinary tract infections.

ACUTE OTITIS MEDIA: For the treatment of acute otitis media in children due to susceptible strains of *Haemophilus influenzae* or *Streptococcus pneumoniae* when in the judgment of the physician Septra offers some advantage over the use of other antimicrobial agents. Limited clinical information is presently available on the effectiveness of treatment of otitis media with Septra when the infection is due to *Haemophilus influenzae* resistant to ampicillin. To date, there are limited data on the safety of repeated use of Septra in children under two years of age. Septra is not indicated for prophylactic or prolonged administration in otitis media at any age.

SHIGELLOSIS: For the treatment of enteritis caused by susceptible strains of *Shigella flexneri* and *Shigella sonnei* when antibacterial therapy is indicated.

PNEUMOCYSTIS CARINII PNEUMONITIS: For the treatment of documented *Pneumocystis carinii* pneumonitis. To date, this drug has been tested only in patients 9 months to 16 years of age who were immunosuppressed by cancer therapy.

CONTRAINDICATIONS: Hypersensitivity to trimethoprim or sulfonamides. Pregnancy and during the nursing period. Infants less than two months of age.

WARNINGS: SEPTRA SHOULD NOT BE USED IN THE TREATMENT OF STREPTOCOCCAL PHARYNGITIS.

Clinical studies have documented that patients with Group A β -hemolytic streptococcal tonsillopharyngitis have a greater incidence of bacteriologic failure when treated with Septra than do those patients treated with penicillin as evidenced by failure to eradicate this organism from the tonsillopharyngeal area.

Deaths associated with administration of sulfonamides have been reported from hypersensitivity reactions, agranulocytosis, aplastic anemia and other blood dyscrasias. Experience with trimethoprim alone is much more limited, but occasional interference with hematopoiesis has been reported as well as an increased incidence of thrombopenia with purpura in elderly patients on certain diuretics, primarily thiazides.

Sore throat, fever, pallor, purpura or jaundice may be early signs of serious blood disorders. Frequent CBCs are recommended; therapy should be discontinued if a significant reduction in the count of any formed blood element is noted.

PRECAUTIONS: Use with caution in patients with impaired renal or hepatic function, possible folate deficiency, severe allergy or bronchial asthma. In glucose-6-phosphate dehydrogenase-deficient individuals, hemolysis may occur (frequently dose-related). During therapy, maintain adequate fluid intake and perform frequent urinalyses with careful microscopic examination and renal function tests, particularly where there is impaired renal function.

Since Septra may prolong prothrombin time in patients on warfarin, coagulation time should be reassessed when Septra is given.

ADVERSE REACTIONS: All major reactions to sulfonamides and trimethoprim are included, even if not reported with Septra. **Blood Dyscrasias:** Agranulocytosis, aplastic anemia, megaloblastic anemia, thrombopenia, leukopenia, hemolytic anemia, purpura, hypoprothrombinemia and methemoglobinemia. **Allergic Reactions:** Erythema multiforme, Stevens-Johnson syndrome, generalized skin eruptions, epidermal necrolysis, urticaria, serum sickness, pruritus, exfoliative dermatitis, anaphylactoid reactions, periorbital edema, conjunctival and scleral injection, photosensitization,

arthralgia and allergic myocarditis. **Gastrointestinal Reactions:** Glossitis, stomatitis, nausea, emesis, abdominal pains, hepatitis, diarrhea and pancreatitis. **C.N.S. Reactions:** Headache, peripheral neuritis, mental depression, convulsions, ataxia, hallucinations, tinnitus, vertigo, insomnia, apathy, fatigue, muscle weakness and nervousness. **Miscellaneous Reactions:** Drug fever, chills, and toxic nephrosis with oliguria and anuria. Periarthritis nodosa and L. E. phenomenon have occurred.

Due to certain chemical similarities to some goitrogens, diuretics (acetazolamide and the thiazides) and oral hypoglycemic agents, sulfonamides have caused rare instances of goiter production, diuresis and hypoglycemia; cross-sensitivity may exist with these agents. In rats, long-term administration of sulfonamides has produced thyroid malignancies.

DOSAGE AND ADMINISTRATION: Not recommended for use in infants less than two months of age.

URINARY TRACT INFECTIONS AND SHIGELLOSIS IN ADULTS AND CHILDREN AND ACUTE OTITIS MEDIA IN CHILDREN:

Adults: The usual adult dosage for the treatment of urinary tract infections is two tablets or four teaspoonfuls (20 ml) every 12 hours for 10 to 14 days. An identical daily dosage is used for 5 days in the treatment of shigellosis.

Children: The recommended dose for children with urinary tract infections or acute otitis media is 8 mg/kg trimethoprim and 40 mg/kg sulfamethoxazole per 24 hours, given in two divided doses every 12 hours for 10 days. An identical daily dosage is used for 5 days in the treatment of shigellosis. The following table is a guideline for the attainment of this dosage using Septra Tablets or Suspension.

Children: Two months of age or older:

Weight		Dose—every 12 hours	
lb	kg	Teaspoonfuls	Tablets
22	10	1 (5 ml)	½
44	20	2 (10 ml)	1
66	30	3 (15 ml)	1½
88	40	4 (20 ml)	2 (or 1 DS tablet)

For patients with renal impairment:

Creatinine Clearance (ml/min)	Recommended Dosage Regimen
Above 30	Usual Standard Regimen
15-30	Half of the usual dosage regimen
Below 15	Use Not Recommended

PNEUMOCYSTIS CARINII PNEUMONITIS:

The recommended dosage for patients with documented *Pneumocystis carinii* pneumonitis is 20 mg/kg trimethoprim and 100 mg/kg sulfamethoxazole per 24 hours given in equally divided doses every 6 hours for 14 days. The following table is a guideline for the attainment of this dosage in children.

Weight		Dose—every 6 hours	
lb	kg	Teaspoonfuls	Tablets
18	8	1 (5 ml)	½
35	16	2 (10 ml)	1
53	24	3 (15 ml)	1½
70	32	4 (20 ml)	2 (or 1 DS tablet)

HOW SUPPLIED: TABLETS, containing 80 mg trimethoprim and 400 mg sulfamethoxazole—bottles of 40, 100, 500 and 1000 tablets; unit dose pack of 100.

ORAL SUSPENSION, containing the equivalent of 40 mg trimethoprim and 200 mg sulfamethoxazole in each teaspoonful (5 ml), cherry flavored—bottle of 450 ml. Also available in double strength, oval-shaped, pink, scored tablets containing 160 mg trimethoprim and 800 mg sulfamethoxazole—Compliance™ Pak of 20, bottle of 60 and unit dose pack of 100.

REFERENCES:

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Burroughs Wellcome Co.
Research Triangle Park
North Carolina 27709

Before prescribing, please consult complete product information, a summary of which follows:

The effectiveness of Valium (diazepam) in long-term use, that is, more than 4 months, has not been assessed by systematic clinical studies. The physician should periodically reassess the usefulness of the drug for the individual patient.

Contraindications: Tablets in children under 6 months of age, known hypersensitivity; acute narrow angle glaucoma; may be used in patients with open angle glaucoma who are receiving appropriate therapy.

Warnings: As with most CNS-acting drugs, caution against hazardous occupations requiring complete mental alertness (e.g., operating machinery, driving). Withdrawal symptoms (similar to those with barbiturates, alcohol) have occurred following abrupt discontinuance (convulsions, tremor, abdominal/muscle cramps, vomiting, sweating). Keep addiction-prone individuals (drug addicts or alcoholics) under careful surveillance because of predisposition to habituation/dependence.

Usage in Pregnancy: Use of minor tranquilizers during first trimester should almost always be avoided because of increased risk of congenital malformations, as suggested in several studies. Consider possibility of pregnancy when instituting therapy; advise patients to discuss therapy if they intend to or do become pregnant.

ORAL: Advise patients against simultaneous ingestion of alcohol and other CNS depressants.

Not of value in treatment of psychotic patients; should not be employed in lieu of appropriate treatment. When using oral form adjunctively in convulsive disorders, possibility of increase in frequency and/or severity of grand mal seizures may require increase in dosage of standard anticonvulsant medication; abrupt withdrawal in such cases may be associated with temporary increase in frequency and/or severity of seizures.

INJECTABLE: To reduce the possibility of venous thrombosis, phlebitis, local irritation, swelling, and, rarely, vascular impairment when used I.V.: inject slowly, taking at least one minute for each 5 mg (1 ml) given; do not use small veins, i.e., dorsum of hand or wrist; use extreme care to avoid intra-arterial administration or extravasation. Do not mix or dilute Valium with other solutions or drugs in syringe or infusion flask. If it is not feasible to administer Valium directly I.V., it may be injected slowly through the infusion tubing as close as possible to the vein insertion.

Administer with extreme care to elderly, very ill, those with limited pulmonary reserve because of possibility of apnea and/or cardiac arrest; concomitant use of barbiturates, alcohol or other CNS depressants increases depression with increased risk of apnea; have resuscitative facilities available. When used with narcotic analgesic eliminate or reduce narcotic dosage at least 1/3, administer in small increments. Should not be administered to patients in shock, coma, acute alcoholic intoxication with depression of vital signs.

Has precipitated tonic status epilepticus in patients treated for petit mal status or petit mal variant status.

Withdrawal symptoms (similar to those with barbiturates, alcohol) have occurred following abrupt discontinuance (convulsions, tremor, abdominal/muscle cramps, vomiting, sweating). Keep addiction-prone individuals under careful surveillance because of predisposition to habituation/dependence. Not recommended for OB use.

Efficacy/safety not established in neonates (age 30 days or less); prolonged CNS depression observed. In children, give slowly (up to 0.25 mg/kg over 3 minutes) to avoid apnea or prolonged somnolence; can be repeated after 15 to 30 minutes. If no relief after third administration, appropriate adjunctive therapy is recommended.

Precautions: If combined with other psychotropics or anticonvulsants, carefully consider individual pharmacologic effects—particularly with known compounds which may potentiate action of Valium (diazepam), i.e., phenothiazines, narcotics, barbiturates, MAO inhibitors and antidepressants. Protective measures indicated in highly anxious patients with accompanying depression who may have suicidal tendencies. Observe usual precautions in impaired hepatic function; avoid accumulation in patients with compromised kidney function. Limit oral dosage to smallest effective amount in elderly and debilitated to preclude ataxia or oversedation (initially 2 to 2½ mg once or twice daily, increasing gradually as needed or tolerated).

INJECTABLE: Although promptly controlled, seizures may return; readminister if necessary, not recommended for long-term maintenance therapy. Laryngospasm/increased cough reflex are possible during peroral endoscopic procedures; use topical anesthetic, have necessary countermeasures available. Hypotension or muscular weakness possible, particularly when used with narcotics, barbiturates or alcohol. Use lower doses (2 to 5 mg) for elderly/debilitated.

Adverse Reactions: Side effects most commonly reported were drowsiness, fatigue, ataxia. Infrequently encountered were confusion, constipation, depression, diplopia, dysarthria, headache, hypotension, incontinence, jaundice, changes in libido, nausea, changes in salivation, skin rash, slurred speech, tremor, urinary retention, vertigo, blurred vision. Paradoxical reactions such as acute hyperexcited states, anxiety, hallucinations, increased muscle spasticity, insomnia, rage, sleep disturbances and stimulation have been reported; should these occur, discontinue drug.

Because of isolated reports of neutropenia and jaundice, periodic blood counts, liver function tests advisable during long-term therapy. Minor changes in EEG patterns, usually low-voltage fast activity, have been observed in patients during and after Valium (diazepam) therapy and are of no known significance.

INJECTABLE: Venous thrombosis/phlebitis at injection site, hypoactivity, syncope, bradycardia, cardiovascular collapse, nystagmus, urticaria, hiccups, neutropenia.

In peroral endoscopic procedures, coughing, depressed respiration, dyspnea, hyperventilation, laryngospasm/pain in throat or chest have been reported.

Management of Overdosage: Manifestations include somnolence, confusion, coma, diminished reflexes. Monitor respiration, pulse, blood pressure, employ general supportive measures, I.V. fluids, adequate airway. Use levaterenol or metaraminol for hypotension, caffeine and sodium benzoate for CNS-depressive effects. Dialysis is of limited value.

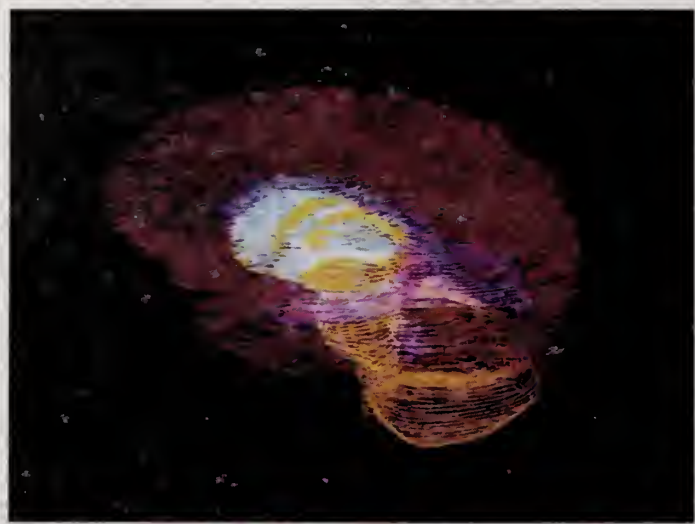
Supplied: Tablets, 2 mg, 5 mg and 10 mg, bottles of 100 and 500; Tel-E-Dose® (unit dose) packages of 100, available in trays of 4 reverse-numbered boxes of 25, and in boxes containing 10 strips of 10; Prescription Paks of 50, available singly and in trays of 10. Ampuls, 2 ml, boxes of 10, Vials, 10 ml, boxes of 1; Tel-E-Ject® (disposable syringes), 2 ml, boxes of 10. Each ml contains 5 mg diazepam, compounded with 40% propylene glycol, 10% ethyl alcohol, 5% sodium benzoate and benzoic acid as buffers, and 1.5% benzyl alcohol as preservative.



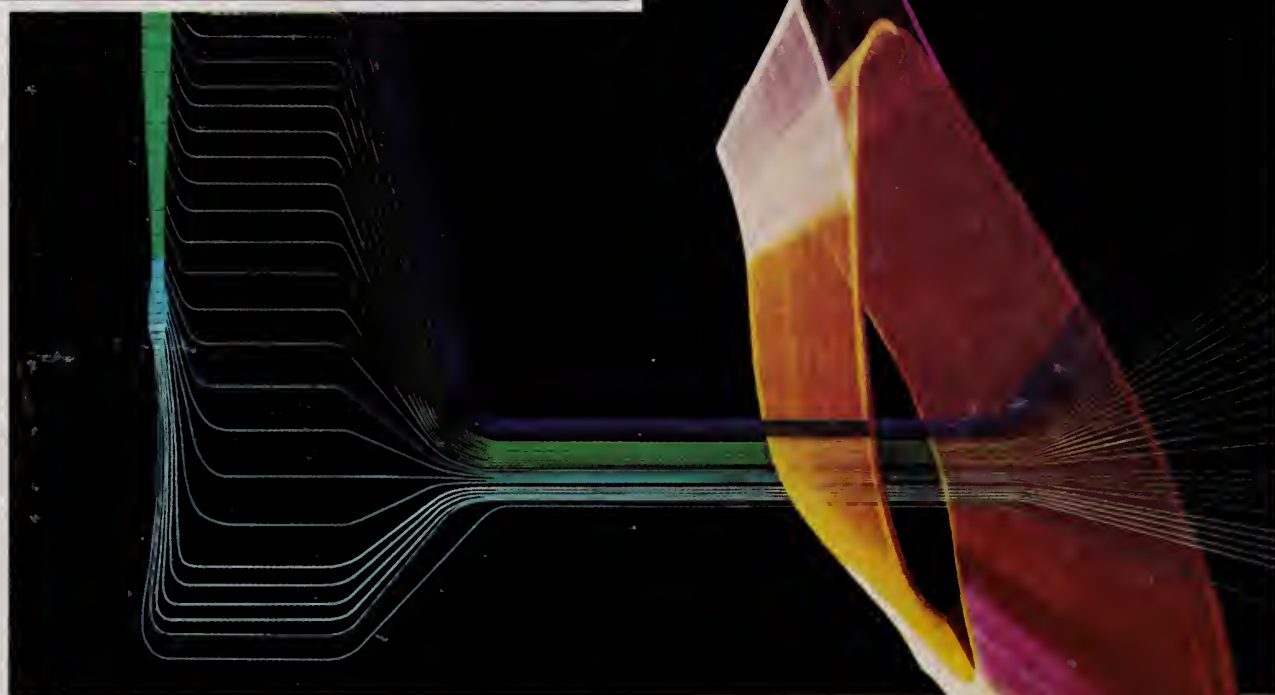
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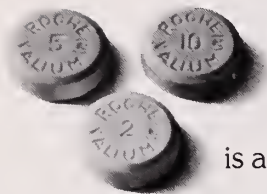
CARTAS AL EDITOR

ABSTRACTOS - CURSOS - NOTICIAS

EKG OF THE MONTH

INDICE PAGINA 98

A character all its own.



Valium (diazepam/Roche)
is a benzodiazepine with a
character all its own.

Pharmacologically, it is a potent skeletal muscle relaxant and anticonvulsant (in adjunctive use), as well as an antianxiety agent. Pharmacokinetically, only Valium provides active diazepam as well as the active metabolites 3-hydroxydiazepam, desmethyldiazepam and oxazepam.

But the individual character of Valium is even more apparent clinically than pharmacokinetically. And far more significant. That's because of the patient response obtained with Valium. A response which brings a calmer frame of mind. A response which has a pronounced effect on the somatic symptoms of anxiety, particularly muscular tension. A response which helps the patient feel more like himself again because of the way Valium reduces the overwhelming symptoms of anxiety and psychic tension.

Another important aspect of the clinical character of Valium is safety. Though drowsiness, ataxia and fatigue are possible, these and more serious side effects are rarely a problem. Of course, as with all CNS-acting drugs, patients taking Valium should be cautioned against driving, operating dangerous machinery or the simultaneous ingestion of alcohol.

Unquestionably, many psychotherapeutic agents, including other benzodiazepines, have antianxiety effects. But one fact remains: you get a certain kind of patient response with Valium. It's a response you want. A response you know. A response you trust as part of your overall management of anxiety and psychic tension.

Valium® diazepam/Roche

2-mg, 5-mg, 10-mg scored tablets
a prudent choice in psychic
tension and anxiety

Before prescribing, please consult complete product information, a summary of which follows:

Indications: Tension and anxiety states; somatic complaints which are concomitants of emotional factors; psychoneurotic states manifested by tension, anxiety, apprehension, fatigue, depressive symptoms or agitation; symptomatic relief of acute agitation, tremor, delirium tremens and hallucinosis due to acute alcohol withdrawal; adjunctively in skeletal muscle spasm due to reflex spasm to local pathology; spasticity caused by upper motor neuron disorders; athetosis; stiff-man syndrome; convulsive disorders (not for sole therapy).

The effectiveness of Valium (diazepam/Roche) in long-term use, that is, more than 4 months, has not been assessed by systematic clinical studies. The physician should periodically reassess the usefulness of the drug for the individual patient.

Contraindicated: Known hypersensitivity to the drug. Children under 6 months of age. Acute narrow angle glaucoma; may be used in patients with open angle glaucoma who are receiving appropriate therapy.

Warnings: Not of value in psychotic patients. Caution against hazardous occupations requiring complete mental alertness. When used adjunctively in convulsive disorders, possibility of increase in frequency and/or severity of grand mal seizures may require increased dosage of standard anticonvulsant medication; abrupt withdrawal may be associated with temporary increase in frequency and/or severity of seizures. Advise against simultaneous ingestion of alcohol and other CNS depressants. Withdrawal symptoms (similar to those with barbiturates and alcohol) have occurred following abrupt discontinuance (convulsions, tremor, abdominal and muscle cramps, vomiting and sweating). Keep addiction-prone individuals under careful surveillance because of their predisposition to habituation and dependence.

Usage in Pregnancy: Use of minor tranquilizers during first trimester should almost always be avoided because of increased risk of congenital malformations as suggested in several studies. Consider possibility of pregnancy when instituting therapy; advise patients to discuss therapy if they intend to or do become pregnant.

Precautions: If combined with other psychotropics or anticonvulsants, consider carefully pharmacology of agents employed; drugs such as phenothiazines, narcotics, barbiturates, MAO inhibitors and other antidepressants may potentiate its action. Usual precautions indicated in patients severely depressed, or with latent depression, or with suicidal tendencies. Observe usual precautions in impaired renal or hepatic function. Limit dosage to smallest effective amount in elderly and debilitated to preclude ataxia or oversedation.

Side Effects: Drowsiness, confusion, diplopia, hypotension, changes in libido, nausea, fatigue, depression, dysarthria, jaundice, skin rash, ataxia, constipation, headache, incontinence, changes in salivation, slurred speech, tremor, vertigo, urinary retention, blurred vision. Paradoxical reactions such as acute hyperexcited states, anxiety, hallucinations, increased muscle spasticity, insomnia, rage, sleep disturbances, stimulation have been reported; should these occur, discontinue drug. Isolated reports of neutropenia, jaundice; periodic blood counts and liver function tests advisable during long-term therapy.

Dosage: Individualize for maximum beneficial effect. *Adults:* Tension, anxiety and psychoneurotic states, 2 to 10 mg b.i.d. to q.i.d.; alcoholism, 10 mg t.i.d. or q.i.d. in first 24 hours, then 5 mg t.i.d. or q.i.d. as needed; adjunctively in skeletal muscle spasm, 2 to 10 mg t.i.d. or q.i.d.; adjunctively in convulsive disorders, 2 to 10 mg b.i.d. to q.i.d. *Geriatric or debilitated patients:* 2 to 2½ mg, 1 or 2 times daily initially, increasing as needed and tolerated. (See Precautions.) *Children:* 1 to 2½ mg t.i.d. or q.i.d. initially, increasing as needed and tolerated (not for use under 6 months).

Supplied: Valium® (diazepam) Tablets, 2 mg, 5 mg and 10 mg—bottles of 100 and 500; Tel-E-Dose® packages of 100, available in trays of 4 reverse-numbered boxes of 25, and in boxes containing 10 strips of 10; Prescription Paks of 50, available singly and in trays of 10.



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The heart of the matter in hypertension is the kidney

The kidney—not the heart—is the key to long-term arterial pressure control. Diuretics help the kidney excrete sodium, reduce fluid volume and lower blood pressure.

No diuretic blocks sodium retention longer than Hygroton.

In mild hypertension low-dose Hygroton 25 mg. An effective, conservative therapy.

In mild hypertension

Low-dose

Hygroton[®] 25 mg. one a day

(chlorthalidone USP)

Gets to the heart of the matter... simply

BRIEF SUMMARY

Indications: Hypertension, adjunctive therapy in edema.

Contraindications: Anuria, hypersensitivity to chlorthalidone or other sulfonamide-derived drugs.

Warnings: Should be used with caution in severe renal disease, impaired hepatic function or progressive liver disease. May add to or potentiate the action of other antihypertensive drugs. Sensitivity reactions may occur in patients with a history of allergy or bronchial asthma. There is a possibility of exacerbation or activation of systemic lupus erythematosus with thiazides, which are related to chlorthalidone. This has not been reported with chlorthalidone. Thiazides cross the placental barrier and appear in cord blood. Use in pregnant women requires that the anticipated benefits of the drug be weighed against possible hazards to the fetus. These hazards include fetal or neonatal jaundice, thrombocytopenia, and possibly other adverse reactions which have occurred in the adult. In nursing mothers, thiazides cross the placental barrier and appear in breast milk. If use of the drug is essential, the patient should stop nursing.

Precautions: Periodic determination of serum electrolytes to detect possible electrolyte imbalance should be performed at appropriate intervals. All patients receiving chlorthalidone should be observed for clinical signs of fluid or electrolyte imbalance, namely, hyponatremia, hypochloremic alkalosis, and hypokalemia. Serum and urine electrolyte determinations are particularly important when the patient is vomiting excessively or receiving parenteral fluids. Medication such as digitalis may also influence serum electrolytes. Hypokalemia may develop with chlorthalidone as with any other potent diuretic, especially with brisk diuresis, when severe cirrhosis is present, or during concomitant use of corticosteroids or ACTH. Interference with adequate oral electrolyte intake will also contribute to hypokalemia. Digitalis therapy may exaggerate metabolic effects of hypokalemia especially with reference to myocardial activity. Any chloride deficit is generally mild and usually does not require specific treatment except under extraordinary circumstances (as in liver disease or renal disease). Dilutional hyponatremia may occur in edematous

patients in hot weather. Hyperuricemia may occur or not be precipitated in certain patients. Insulin requirements in diabetic patients may be increased, decreased, or unchanged and latent diabetes mellitus may become manifest. Chlorthalidone and related drugs may increase the responsiveness to tubocurarine. The antihypertensive effects of the drug may be enhanced in the post-sympathectomy patient. Chlorthalidone and related drugs may decrease arterial responsiveness to norepinephrine. If progressive renal impairment becomes evident, as indicated by a rising nonprotein nitrogen or blood urea nitrogen, a careful reappraisal of therapy is necessary with consideration given to withholding or discontinuing diuretic therapy. Chlorthalidone and related drugs may decrease serum PBI levels without signs of thyroid disturbance.

Adverse Reactions: Anorexia, gastric irritation, nausea, vomiting, cramping, diarrhea, constipation, jaundice (intrahepatic cholestatic jaundice), pancreatitis, dizziness, vertigo, paresthesias, headache, xanthopsia, leukopenia, agranulocytosis, thrombocytopenia, aplastic anemia, purpura, photosensitivity, rash, urticaria, necrotizing angitis (vasculitis) (cutaneous), scurvy, Lyell's syndrome (toxic epidermal necrolysis). Orthostatic hypotension may occur and may be aggravated by alcohol, barbiturates or narcotics. Other adverse reactions include hyperglycemia, glycosuria, hyperuricemia, muscle spasm, weakness, restlessness, impotence. Whenever adverse reactions are moderate or severe, chlorthalidone dosage should be reduced or therapy withdrawn.

Usual Dose: One tablet daily.

How Supplied: Tablets—100 mg. (white, scored), 50 mg. (aqua) and 25 mg. (peach) in bottles of 100 and 1000, unit-dose blister packs, boxes of 100 (10 x 10 strips). Also 100 mg. and 50 mg. in PAKs of 28 tablets, boxes of 5.

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In recurrent urinary tract infections



Septtra[®] DS

Each tablet contains:
160 mg trimethoprim and 800 mg sulfamethoxazole

B.I.D.

**where
the action is.**

JUN



In the kidney

Septra DS provides effective anti-bacterial action in the kidneys, via urine and blood, against susceptible strains of E coli, Klebsiella-Enterobacter, Proteus mirabilis, Proteus vulgaris and Proteus morganii.

The high degree of efficacy of Septra DS was confirmed in a study of 59 patients with recurrent pyelonephritis. All patients had upper urinary tract disease as evidenced by fever $\geq 100.4^{\circ}$ F and/or flank pain, and $\geq 10^5$ organisms/ml of urine. After two weeks' therapy and up to seven days post-therapy, Septra achieved bacteriologic cure ($\leq 10,000$ organisms/ml of urine) in 91.5% of patients.¹

And during the critical "recurrence" period from one to four weeks post-therapy, this excellent response rate was well maintained. Of the 53 patients evaluated at that time, 51 (96.2%) were still infection free.¹

Unlike many other antibacterials for the treatment of urinary tract infections, Septra DS is administered on a convenient b.i.d. dosage schedule.

In the bladder

What makes Septra DS good for the tough areas—the kidneys—makes it good for the not-so-tough. Septra DS provides antibacterial action in the bladder, via urine and blood, against susceptible strains of major pathogens that cause recurrent cystitis.

And along the route to recurrence

During therapy, Septra DS diffuses into vaginal fluid² and into the bowel.^{3,4} By eliminating potential uropathogens from the fecal flora, and bathing the periurethral area in an "antibacterial" vaginal fluid, Septra DS helps block the most common route to reinfection in women.

Maintain adequate fluid intake and perform frequent urinalyses with careful microscopic examination during therapy. Septra is contraindicated in children under two months old.

Please see prescribing information on next page.



Burroughs Wellcome Co.
Research Triangle Park
North Carolina 27709

Septra® DS B.I.D.

Each tablet contains: 160 mg trimethoprim and 800 mg sulfamethoxazole

Septra® Suspension B.I.D.

Each teaspoonful (5 ml) contains: 40 mg trimethoprim and 200 mg sulfamethoxazole

Septra® DS Tablets Double Strength

Septra® Tablets

Septra® Suspension

INDICATIONS AND USAGE:

URINARY TRACT INFECTIONS: For the treatment of urinary tract infections due to susceptible strains of the following organisms: *Escherichia coli*, *Klebsiella-Enterobacter*, *Proteus mirabilis*, *Proteus vulgaris*, *Proteus morganii*. It is recommended that initial episodes of uncomplicated urinary tract infections be treated with a single effective antibacterial agent rather than the combination.

NOTE: Currently, the increasing frequency of resistant organisms is a limitation of the usefulness of all antibacterial agents, especially in the treatment of these urinary tract infections.

ACUTE OTITIS MEDIA: For the treatment of acute otitis media in children due to susceptible strains of *Haemophilus influenzae* or *Streptococcus pneumoniae* when in the judgment of the physician Septra offers some advantage over the use of other antimicrobial agents. Limited clinical information is presently available on the effectiveness of treatment of otitis media with Septra when the infection is due to *Haemophilus influenzae* resistant to ampicillin. To date, there are limited data on the safety of repeated use of Septra in children under two years of age. Septra is not indicated for prophylactic or prolonged administration in otitis media at any age.

SHIGELLOSIS: For the treatment of enteritis caused by susceptible strains of *Shigella flexneri* and *Shigella sonnei* when antibacterial therapy is indicated.

PNEUMOCYSTIS CARINII PNEUMONITIS: For the treatment of documented *Pneumocystis carinii* pneumonitis. To date, this drug has been tested only in patients 9 months to 16 years of age who were immunosuppressed by cancer therapy.

CONTRAINDICATIONS: Hypersensitivity to trimethoprim or sulfonamides. Pregnancy and during the nursing period. Infants less than two months of age.

WARNINGS: SEPTRA SHOULD NOT BE USED IN THE TREATMENT OF STREPTOCOCCAL PHARYNGITIS.

Clinical studies have documented that patients with Group A β -hemolytic streptococcal tonsillitis have a greater incidence of bacteriologic failure when treated with Septra than do those patients treated with penicillin as evidenced by failure to eradicate this organism from the tonsillopharyngeal area.

Deaths associated with administration of sulfonamides have been reported from hypersensitivity reactions, agranulocytosis, aplastic anemia and other blood dyscrasias. Experience with trimethoprim alone is much more limited, but occasional interference with hematopoiesis has been reported as well as an increased incidence of thrombopenia with purpura in elderly patients on certain diuretics, primarily thiazides.

Sore throat, fever, pallor, purpura or jaundice may be early signs of serious blood disorders. Frequent CBCs are recommended; therapy should be discontinued if a significant reduction in the count of any formed blood element is noted.

PRECAUTIONS: Use with caution in patients with impaired renal or hepatic function, possible folate deficiency, severe allergy or bronchial asthma. In glucose-6-phosphate dehydrogenase-deficient individuals, hemolysis may occur (frequently dose-related). During therapy, maintain adequate fluid intake and perform frequent urinalyses with careful microscopic examination and renal function tests, particularly where there is impaired renal function.

Since Septra may prolong prothrombin time in patients on warfarin, coagulation time should be reassessed when Septra is given.

ADVERSE REACTIONS: All major reactions to sulfonamides and trimethoprim are included, even if not reported with Septra. **Blood Dyscrasias:** Agranulocytosis, aplastic anemia, megaloblastic anemia, thrombopenia, leukopenia, hemolytic anemia, purpura, hypoprothrombinemia and methemoglobinemia. **Allergic Reactions:** Erythema multiforme, Stevens-Johnson syndrome, generalized skin eruptions, epidermal necrolysis, urticaria, serum sickness, pruritus, exfoliative dermatitis, anaphylactoid reactions, periorbital edema, conjunctival and scleral injection, photosensitization,

arthralgia and allergic myocarditis. **Gastrointestinal Reactions:** Glossitis, stomatitis, nausea, emesis, abdominal pains, hepatitis, diarrhea and pancreatitis. **C.N.S. Reactions:** Headache, peripheral neuritis, mental depression, convulsions, ataxia, hallucinations, tinnitus, vertigo, insomnia, apathy, fatigue, muscle weakness and nervousness. **Miscellaneous Reactions:** Drug fever, chills, and toxic nephrosis with oliguria and anuria. Periarthritis nodosa and L. E. phenomenon have occurred.

Due to certain chemical similarities to some goitrogens, diuretics (acetazolamide and the thiazides) and oral hypoglycemic agents, sulfonamides have caused rare instances of goiter production, diuresis and hypoglycemia; cross-sensitivity may exist with these agents. In rats, long-term administration of sulfonamides has produced thyroid malignancies.

DOSAGE AND ADMINISTRATION: Not recommended for use in infants less than two months of age.

URINARY TRACT INFECTIONS AND SHIGELLOSIS IN ADULTS AND CHILDREN AND ACUTE OTITIS MEDIA IN CHILDREN:

Adults: The usual adult dosage for the treatment of urinary tract infections is two tablets or four teaspoonfuls (20 ml) every 12 hours for 10 to 14 days. An identical daily dosage is used for 5 days in the treatment of shigellosis.

Children: The recommended dose for children with urinary tract infections or acute otitis media is 8 mg/kg trimethoprim and 40 mg/kg sulfamethoxazole per 24 hours, given in two divided doses every 12 hours for 10 days. An identical daily dosage is used for 5 days in the treatment of shigellosis. The following table is a guideline for the attainment of this dosage using Septra Tablets or Suspension.

Children: Two months of age or older:

Weight		Dose —every 12 hours	
lb	kg	Teaspoonfuls	Tablets
22	10	1 (5 ml)	½
44	20	2 (10 ml)	1
66	30	3 (15 ml)	1½
88	40	4 (20 ml)	2 (or 1 DS tablet)

For patients with renal impairment:

Creatinine Clearance (ml/min)	Recommended Dosage Regimen
Above 30	Usual Standard Regimen
15-30	Half of the usual dosage regimen
Below 15	Use Not Recommended

PNEUMOCYSTIS CARINII PNEUMONITIS:

The recommended dosage for patients with documented *Pneumocystis carinii* pneumonitis is 20 mg/kg trimethoprim and 100 mg/kg sulfamethoxazole per 24 hours given in equally divided doses every 6 hours for 14 days. The following table is a guideline for the attainment of this dosage in children.

Weight		Dose —every 6 hours	
lb	kg	Teaspoonfuls	Tablets
18	8	1 (5 ml)	½
35	16	2 (10 ml)	1
53	24	3 (15 ml)	1½
70	32	4 (20 ml)	2 (or 1 DS tablet)

HOW SUPPLIED: TABLETS, containing 80 mg trimethoprim and 400 mg sulfamethoxazole—bottles of 40, 100, 500 and 1000 tablets; unit dose pack of 100.

ORAL SUSPENSION, containing the equivalent of 40 mg trimethoprim and 200 mg sulfamethoxazole in each teaspoonful (5 ml), cherry flavored—bottle of 450 ml. Also available in double strength, oval-shaped, pink, scored tablets containing 160 mg trimethoprim and 800 mg sulfamethoxazole—Compliance™ Pak of 20, bottle of 60 and unit dose pack of 100.

REFERENCES:

(1) Data on file, Burroughs Wellcome Co. (2) Stamey TA, Condly M: The diffusion and concentration of trimethoprim in human vaginal fluid, in *Trimethoprim/Sulfamethoxazole: A Compilation of Clinical and Pharmacodynamic Studies in Chronic and Recurrent Urinary Tract Infections*. Science & Medicine Publishing Co, 1975, p 13. (3) Näff H: *Pathol Microbiol* 37:1, 1971. (4) Moorhouse EC, Farrell W: *J Med Microbiol* 6:249, 1973.



Burroughs Wellcome Co.
Research Triangle Park
North Carolina 27709

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ASOCIACION MEDICA DE PUERTO RICO

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El Boletín se publica mensualmente. El precio de suscripción es de \$10.00 al año. Todo material de anuncio está sujeto a aprobación por la Junta Editora. La tarifa de precios para anuncios será suministrada a solicitud. Copia del anuncio debe ser recibida el día primero del mes que precede al mes de publicación. Representante de anuncios nacionales es la State Medical Journal Advt. Bureau, 711 South Blvd., Oak Park, Illinois 60302.

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ASOCIACION MEDICA DE PUERTO RICO

I N D I C E

MARZO 1980

VOLUMEN 72
NUMERO 3

- * Expected Risk of Coronary Heart Disease in Puerto Rican Men 98
Raúl Costas, Jr., MD, Mario R. García Palmieri, MD, Mercedes Cruz Vidal, MD y Paul Sorlie, MS

In this issue, Costas and co-workers present the information collected in 9824 men residing in 3 urban and 4 rural areas in Puerto Rico. The study group has been followed prospectively for 8 years to assess the prevalence of risk factors and to study their effects on the subsequent development of coronary heart disease. Using this data, and multiple logistic function analysis the authors estimated the risk for Puerto Rican urban and rural men 50 to 60 years old developing coronary heart disease over an eight year period. The risk is presented in different tables that will enable the practicing physician to identify those individuals at a higher risk of developing coronary heart disease.

- * BCG vs Isoniazid in the Prevention of Tuberculosis 111
José E. Sifontes, MD, FAAP

La reducción de la morbilidad y mortalidad por tuberculosis en Puerto Rico ha sido uno de los mejores logros de Salud Pública en nuestro país. El Dr. José Sifontes, junto con otros eminentes científicos, participó activamente en los estudios de profilaxis y prevención en los años 1949-1951. En esta edición del Boletín se presentan en forma concisa los resultados de la vacunación con BCG y profilaxis con isoniazida llevado a cabo en los años antes mencionados. Los resultados que Sifontes presenta sirvieron de base para que en Puerto Rico se adoptara en el 1959 la isoniazida como método de elección para la prevención de tuberculosis.

- * New Advances in the Immunodiagnosis of Parasitic Infections
II. Counterelectrophoresis 117
George V. Hillyer, PhD and Irving G. Kagan, PhD

In this review article Hillyer and Kagan present a complete review of counterelectrophoresis in the diagnosis of parasitic infections. Although this test is rapid, and requires small amounts of inexpensive reactants, experience is required to interpret the results. Artifacts are often observed in the form of precipitate lines near the serum wells, particularly when crude antigens are used. For those interested in the clinical application of counterelectrophoresis, the author included in their review several tables outlining the use of this test and the serodiagnosis of different parasitic infections.

*	Flavobacterium, Infective Endocarditis and Prosthetic Heart Valve	126
	<i>Charles D. Johnson, MD</i>	

In this issue Johnson reports a 38-year old male with *Flavobacterium* infective endocarditis in a prosthetic mitral valve. According to the author this is the second case reported in the literature. *Flavobacterium* is an aerobic gram negative rod widely distributed in water, soil and dairy products. Its antibiotic susceptibility is unique, generally sensitive to erythromycin, vancomycin and neomycin. An excellent review of the literature emphasizing prevention, neurologic complications and therapy is included.

*	Comunicación Breve: Pediatría, el Patito Feo	135
	<i>Eduardo Vachier, MD</i>	

*	Revisión de Textos Nuevos - Glucagón en Gastroenterología	137
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*	EKG of the Month	159
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NOTA DEL EDITOR

Entre los objetivos principales de la Junta Editora del Boletín de la Asociación Médica de Puerto Rico, está el de modificar el formato y el contenido del Boletín de tal manera que responda más a las necesidades informativas de la clase médica de Puerto Rico. De igual forma el Boletín es el medio informativo más importante mediante el cual se publican localmente resúmenes médicos, ideas originales o trabajos de repaso sometidos por profesionales médicos y paramédicos.

No existe mejor método de enseñanza y docencia que el tener que preparar, redactar y evaluar un artículo para publicación. Esta experiencia ayuda al autor a organizar ideas, evaluar críticamente la información disponible y a expresar verbalmente sus conocimientos en la materia. Es por estas razones que el Boletín de la Asociación Médica de Puerto Rico podría colaborar en el entrenamiento, educación y formación de futuros médicos y especialistas.

Con este propósito publicamos una sección en el Boletín, titulada: "Gráfica", cuyo objetivo es ilustrar por medios fotográficos, condiciones patológicas de interés clínico general; ilustración radiográfica de úlcera péptica, electrocardiogramas poco usuales, radiografía de tórax ilustrando un aneurisma disectante, etc.

A nombre de la Junta Editora invito a todos los compañeros en la clase médica a someter ilustraciones de interés clínico para publicación en el Boletín. Cada ilustración debe estar acompañada por una breve pero pertinente descripción clínica, además de 1 o 2 preguntas con varias posibles contestaciones. Estas ilustraciones y su contenido serán evaluadas por la Junta Editora. Todo comentario y sugerencia relacionados con el estilo y formato, serán devueltas al autor en forma de crítica constructiva. De esta manera él tendrá una evaluación objetiva de su trabajo.

La Asociación Médica de Puerto Rico premiará con \$25.00 el esfuerzo de todo autor principal cuyo trabajo sea publicado mensualmente en la Sección Gráfica.

Firmemente creemos que de esta manera el Boletín y la Asociación Médica estarán colaborando directamente en la formación profesional de nuestros colegas.

*Juan M. Aranda, MD, FACC
Presidente
Junta Editora*

EXPECTED RISK OF CORONARY HEART DISEASE IN PUERTO RICAN MEN

Raúl Costas, Jr., MD, Mario R. García-Palmieri, MD
Mercedes Cruz Vidal, MD y Paul Sorlie, MS

Summary: The risk of developing CHD in 8 years has been estimated for Puerto Rican urban and rural men 50 to 60 years old using levels of blood pressure, serum cholesterol, cigarette smoking, and presence or absence of glucose intolerance. Risk tables enable the physician to delineate more clearly those individuals at high risk either because of risk factors definitely abnormal, or because of evidence of many marginal abnormalities.

Resumen: Se ha calculado el riesgo de desarrollar cardiopatía coronaria en 8 años para varones puertorriqueños de 50 a 60 años de edad y residencia urbana y rural. Este cálculo se basa en los niveles de presión arterial y colesterol sérico y en la presencia o ausencia del hábito de fumar cigarrillos e intolerancia a la glucosa.

Las tablas de riesgo permiten al médico identificar aquellas personas con riesgo mayor, ya sea debido a anormalidades definitivas de los factores de riesgo o a la presencia de anormalidades marginales múltiples.

From the Department of Medicine, University of Puerto Rico School of Medicine and the Division of Heart and Vascular Diseases, Biometrics Research Branch, National Heart, Lung, and Blood Institute, Bethesda, Maryland.

Supported by Contract PH 43-63-620 of the National Heart, Lung, and Blood Institute, U. S. Public Health Service.

Although the incidence of coronary heart disease (CHD) in Puerto Rico is low compared to other countries (1), CHD is the leading cause of death (2). The natural history of the disease is such that clinical manifestations occur usually when the disease is well advanced, resulting in a large number of disabilities and premature deaths, frequently at the ages of greatest productivity of the individual. Clearly one step in the solution of this public health problem would be the early identification of individuals with a high probability of developing clinical manifestations of CHD, so that appropriate intervention might be applied to reduce the incidence of disease.

For many years the personal characteristics of individuals at high risk of developing CHD have been identified in many epidemiological studies. These precursors of CHD - commonly called risk factors - include hypertension, hypercholesterolemia, cigarette smoking, and glucose intolerance (GLI). It is also known that advancing age increases the risk. Risk will vary not only by the level of a particular factor but also according to the presence of other associated abnormalities. In fact, an individual with several "slight" or "borderline" abnormalities could be at a distinctly increased risk of CHD even though none of the factors taken simply would classify him in a high risk category.

Since 1965, 9824 men residing in 3 urban and 4 rural areas of Puerto Rico have been followed prospectively to assess the prevalence of risk factors and their effect on the

subsequent development of CHD. Using the data collected in this study and multiple logistic function analysis the risk of developing CHD over an eight year period for a number of risk factors is estimated and compiled in a series of tables. The purpose of this paper is to present these tables and discuss their use.

Materials and Methods

The details of the study have been presented elsewhere (3). A house to house census of all men 45 to 64 years old was conducted in the urban enumeration districts (ED's) of the municipalities of Bayamón, Guaynabo and Carolina, and the rural ED's of Naranjito, Comerío, Barranquitas and Corozal. Respondents were 80 percent of those given appointments in each area. They were interviewed, using standardized questionnaires, to assess their socioeconomic status, smoking and activity habits, diet, and medical history. A detailed cardiovascular examination, vitalometry, and 12-lead electrocardiogram were performed. Urine was examined for sugar and albumin, and blood for hematocrit, sugar, cholesterol, glycerides and lipoproteins. Laboratory methods used are described elsewhere (4). The blood glucose-urine sugar-diabetes information make up the GLI value (history of diabetes, or blood glucose 120 mg/dl or more, or urine sugar positive or trace).

Individuals found free of CHD at the first examination were followed at subsequent clinic visits at 2 to 3 - year intervals to detect incidence of new disease. At these visits historical and electrocardiographic data were obtained. Clinic records of all incidence cases were reviewed. All interim hospitalizations were reviewed with photocopies of hospital records and EGG's. All deaths were reviewed by autopsy protocols when available, copies of hospital records and EGG's, and interviews with the attending physician or the next of kin as needed. Diagnosis of new CHD was made by the study physicians at special review sessions (5), using standardized criteria deve-

loped for the study (6, 7). All information was key-punched on cards and transferred to magnetic tapes.

Statistical Methodology

The multiple logistic function was chosen as the model to describe the relationship between CHD incidence and characteristics measured at baseline. This model was selected because it fits the data well, and therefore it seems to be a reasonable method to estimate probabilities of CHD. The variables chosen as risk factors for CHD (age, systolic blood pressure (SBP), serum cholesterol (SC), cigarette smoking and GLI) are not necessarily exhaustive of all possible risk factors. A "risk" factor affects the risk or chances of developing disease, but does not exactly predict those who will or will not develop CHD.

The logistic function is described by the following equation:

$$p = 1/(1 + e^{-(\alpha + \beta_1 x_1 + \beta_2 x_2 + \beta_3 x_3 + \beta_4 x_4 + \beta_5 x_5)}) \quad (\text{equation 1})$$

where p is the probability of developing CHD in 8 years.

α and β_i are the intercept and coefficients, and

x_i are the independent variables:

x_1 = age (yr)

x_2 = SBP (mm Hg)

x_3 = SC (mg/dl)

x_4 = cigarette smoking (0 = no, 1 = yes)

TABLE I
Multiple Logistic Function Coefficients of the Risk of Coronary Heart
Disease in 8 Years on Specified Variables Measured at Exam 1
Puerto Rico Heart Health Program
Men 45-64 Years

Variable (units)	Logistic function coefficients	
	Rural	Urban
Age (years)	0.023376	0.024640 *
Systolic blood pressure (mm Hg)	0.020651 **	0.016570 **
Serum cholesterol (mg/dl)	0.002658	0.006966 **
Cigarette smoking (0=no, 1=yes)	0.514755 **	0.465059 **
Glucose intolerance (0=no, 1=yes)	0.322657	0.591538 **
Intercept	-7.829681 **	-8.209912 **
No. CHD cases/population	118/2399	335/5794

* $p < .05$

** $p < .01$

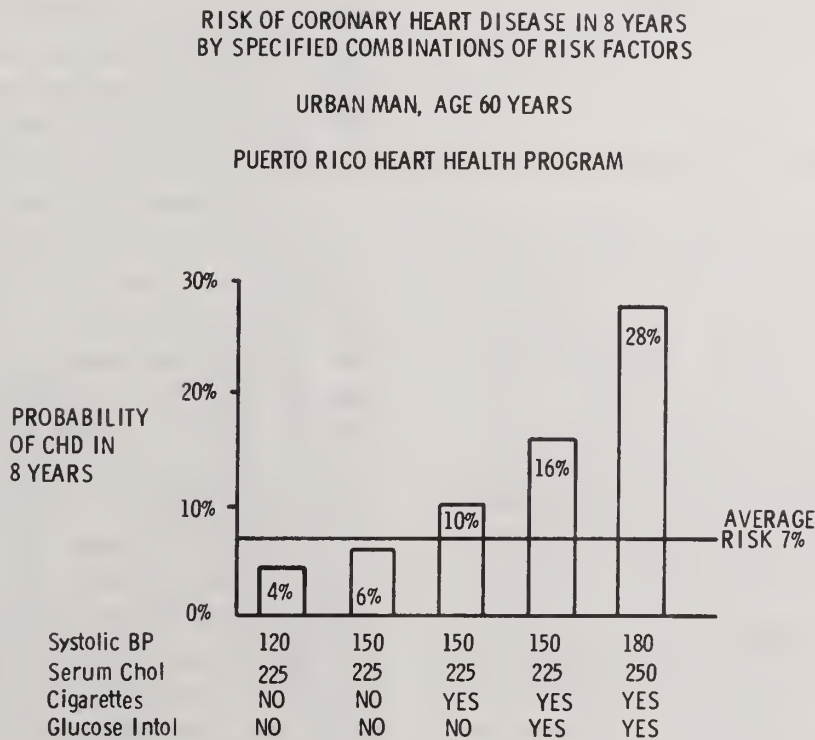
x_5 = glucose intolerance (0 = no, 1 = yes diabetic, or blood sugar 120 mg/dl or more, or urine sugar positive or trace)

If we knew the values of α and β_i , then we would have an equation which would predict the probability of CHD given values of the personal attributes (x_i). Estimates of those coefficients can be made using the iterative least squares approach suggested by Walker and Duncan (8). The estimated coefficients are shown in Table I. The statistical testing of these coefficients indicates whether the net contribution to risk of the particular variable is statistically significant from zero.

As seen in the table, the variables selected for this risk assessment are all statistically significant in the urban area. In the rural area, age, SC, and GLI are not statistically significant. However, the magnitude of the coefficients indicates a risk not too unlike that seen in the urban area. The population is smaller in the rural area, making statistical significance harder to achieve than in the urban area. Because of this, both the rural and urban area have risk functions based on the same baseline attributes.

An assessment of the fit of this multivariate model is made by examining the deciles of risk. Using the estimated coefficients from Table I and equation 1, the probability of CHD

FIGURE 2



is shown in Figure 1. The broken line in the Figure is the expected number of cases based on the model. It is a smooth line which gets steeper at the higher deciles of risk. The solid line indicates the observed number of cases in each decile. This line deviates from the smooth line, but it mostly appears to be a random type of deviation due to variation in the observed number of cases. The two curves generally have the same shape and fall on top of each other, indicating that the fit of the model is good.

Figure 1 also gives an indication of the predictive ability of the model. If the risk factors were perfect predictors, all of the observed cases would appear in the top deciles and no cases would appear in the lower groups. If the factors had no predictive ability, there would

be an equal number of cases in each decile, and the solid line in Figure 1 would be flat. There is considerable predictive ability using the risk factors tested, with 42 percent of the cases in the urban area and 45 percent in the rural occurring in the upper two deciles. Thus, in terms of both model fit and predictability, the logistic function based on the five risk factors appears satisfactory.

The tables of risk presented in this paper are merely convenient tabulations of individual probabilities of CHD using the coefficients in Table I and equation 1. For each combination of level of the five risk factors, a probability was calculated and put in the appropriate section of the table. Of course, given an individual's specific values, a probability based on these values can be calcu-

lated. In the tables the probabilities for given values (or closest values) are easily found.

Description of the Tables

There are six tables (Tables 2 to 7): three for urban men and three for rural. Each of the 3 tables for each group is for a different age at 5-year intervals: viz., 50, 55, and 60 years of age. Each table presents a portion on the left for the individual who does not smoke cigarettes and one on the right for the cigarette smoker. Each portion is divided into an upper section for the individual without GLI and a lower one for the patient with GLI. Each section has a heading of SC values (in mg/dl) reading down and one of SBP values (in mm Hg) reading across. The numbers in the table indicate the percent probability of developing CHD in 8 years according to the specified characteristics.

Use of the Tables

To use the tables an individual's age and values of blood glucose and urine sugar, and history of smoking and diabetes must be known. For example, a rural man aged 50 who does not smoke, has a SBP of 120 mm Hg, a SC of 200 mg/dl, and is not glucose intolerant, when looked up in the tables for his specified values, is found to have a risk of 3. This means that he has a 3 percent chance of developing CHD in the next 8 years. Similarly, a rural man aged 50 years who smokes, has a SBP of 180 mm Hg, a SC of 250 mg/dl, and is not glucose intolerant would have a 15 percent risk of CHD in the next 8 years. For persons whose age is between the 5 year intervals given in the tables or whose SBP or SC value is between

those listed, one can either choose the nearest figure from the tables or use a linear interpolation. In the last example given, if the person's SBP was 190 instead of 180 mm Hg, his expected risk would be approximately 17 percent.

An individual's risk can be compared to the rest of the population by using the "average risk" which is indicated for each area and age group at the top of each table. For example, the average risk for a rural man aged 50 years is 4 percent. If a rural man aged 50 has risk factors yielding a risk of 12 percent, he has three times the risk of subsequent CHD as the average man his same age and area of residence.

Figure 2 shows how the risks from multiple abnormalities mount up. All values are taken from the risk table for a 60-year old urban man. A man from his area and age group who does not smoke, is not glucose intolerant, and has a SBP of 120 mm Hg and a SC of 225 mg/dl will have a risk of developing CHD in 8 years of 4 percent. A man from the same area and age group who does not smoke and is not glucose intolerant, but whose SBP is 150 mm and SC 225 mg will have a risk of 6 percent. An individual with these same numerical values for SBP and SC but who is a cigarette smoker will have an increased risk to 10 percent. If in addition he has GLI, the risk is 16 percent. Finally a 60-year old urban man who smokes cigarettes, is glucose intolerant, and has a SBP of 180 mm Hg and a SC of 250 mg/dl will have a risk of developing CHD in 8 years of 28 percent.

Discussion

The risk estimates in these tables are probably valid for the general Puerto Rican male population. While the Municipalities studied are not a sample of the island, it is

TABLE II
Probability (In Percent) of Developing Coronary Heart Disease in Eight Years According to Specified Characteristics.
Estimates Based on Data from the Puerto Rico Heart Health Program
Rural Man Aged 50 Years
(Average Risk is 4 Percent)

DOES NOT SMOKE CIGARETTES										SMOKES CIGARETTES											
	SERUM CHOLESTEROL (MG/DL)					SYSTOLIC BLOOD PRESSURE (MM HG)					SERUM CHOLESTEROL (MG/DL)					SYSTOLIC BLOOD PRESSURE (MM HG)					
	105	120	135	150	165	180	195	105	120	135	150	165	180	195	105	120	135	150	165	180	195
NO GLUCOSE INTOLERANCE	150	2	2	3	4	5	7	10	150	3	4	5	7	9	12	15					
	175	2	2	3	4	6	8	10	175	3	4	5	7	9	12	16					
	200	2	3	3	5	6	8	11	200	3	4	6	7	10	13	17					
	225	2	3	4	5	7	9	12	225	3	4	6	8	11	14	18					
	250	2	3	4	5	7	9	12	250	4	5	6	8	11	15	19					
	275	2	3	4	6	7	10	13	275	4	5	7	9	12	15	20					
	SERUM CHOLESTEROL (MG/DL)					SYSTOLIC BLOOD PRESSURE (MM HG)					SERUM CHOLESTEROL (MG/DL)					SYSTOLIC BLOOD PRESSURE (MM HG)					
	105	120	135	150	165	180	195	105	120	135	150	165	180	195	105	120	135	150	165	180	195
YES GLUCOSE INTOLERANCE	150	2	3	4	6	7	10	13	150	4	5	7	9	12	15	20					
	175	2	3	4	6	8	10	14	175	4	5	7	9	12	16	21					
	200	3	3	5	6	8	11	14	200	4	6	8	10	13	17	22					
	225	3	4	5	7	9	12	15	225	4	6	8	11	14	18	23					
	250	3	4	5	7	9	12	16	250	5	6	9	11	15	19	24					
	275	3	4	6	8	10	13	17	275	5	7	9	12	16	20	26					

TABLE III

Probability (In Percent) of Developing Coronary Heart Disease in Eight Years According to Specified Characteristics.
Estimates Based on Data From the Puerto Rico Heart Health Program

Urban Man Aged 50 Years
(Average Risk is 5 Percent)

		DOES NOT SMOKE CIGARETTES								SMOKES CIGARETTES							
		SYSTOLIC BLOOD PRESSURE (MM HG)								SYSTOLIC BLOOD PRESSURE (MM HG)							
	SERUM CHOLESTEROL (MG/DL)	105	120	135	150	165	180	195		SERUM CHOLESTEROL (MG/DL)	105	120	135	150	165	180	195
		1	2	2	3	4	5	6		150	2	3	4	5	6	8	10
NO	175	2	2	3	4	5	6	7		175	3	4	4	6	7	9	11
GLUCOSE	200	2	3	3	4	5	7	9		200	3	4	5	7	8	11	13
INTOLERANCE	225	2	3	4	5	6	8	10		225	4	5	6	8	10	12	15
	250	3	4	5	6	8	10	12		250	5	6	7	9	12	14	18
	275	3	4	6	7	9	11	14		275	5	7	9	11	13	17	20
		SYSTOLIC BLOOD PRESSURE (MM HG)								SYSTOLIC BLOOD PRESSURE (MM HG)							
		SERUM CHOLESTEROL (MG/DL)	105	120	135	150	165	180	195	SERUM CHOLESTEROL (MG/DL)	105	120	135	150	165	180	195
YES	150	3	3	4	5	7	9	11		150	4	5	7	8	11	13	16
	175	3	4	5	6	8	10	13		175	5	6	8	10	12	15	19
GLUCOSE	200	4	5	6	8	9	12	15		200	6	7	9	11	14	18	21
INTOLERANCE	225	4	6	7	9	11	14	17		225	7	9	11	13	17	20	25
	250	5	7	8	10	13	16	20		250	8	10	13	16	19	23	28
	275	6	8	10	12	15	18	22		275	9	12	15	18	22	26	32

TABLE IV

Probability (In Percent) of Developing Coronary Heart Disease in Eight Years According to Specified Characteristics.
Estimates Based on Data from the Puerto Rico Heart Health Program

Rural Man Aged 55 Years
(Average Risk is 5 Percent)

DOES NOT SMOKE CIGARETTES										SMOKES CIGARETTES																																																																														
	SYSTOLIC BLOOD PRESSURE (MM HG)					SYSTOLIC BLOOD PRESSURE (MM HG)					SYSTOLIC BLOOD PRESSURE (MM HG)					SYSTOLIC BLOOD PRESSURE (MM HG)																																																																								
	CHOLESTEROL					CHOLESTEROL					CHOLESTEROL					CHOLESTEROL																																																																								
	SERUM (MG/DL)	105	120	135	150	165	180	195	SERUM (MG/DL)	105	120	135	150	165	180	195	SERUM (MG/DL)	105	120	135	150	165	180	195	SERUM (MG/DL)	105	120	135	150	165	180	195																																																								
NO GLUCOSE INTOLERANCE	150	2	2	3	5	6	8	11	150	3	4	6	7	10	13	17	175	3	4	6	8	10	14	18	200	2	3	4	5	7	9	12	200	3	5	6	8	11	14	19	225	2	3	4	5	7	10	13	225	4	5	7	9	12	15	20	250	2	3	4	6	8	10	14	250	4	5	7	9	12	16	21	275	3	3	5	6	8	11	14	275	4	6	8	10	13	17	22
YES GLUCOSE INTOLERANCE	150	3	3	5	6	8	11	14	150	4	6	7	10	13	17	22	175	4	6	8	10	14	18	23	200	3	4	5	7	9	12	16	200	5	6	8	11	15	19	24	225	3	4	6	7	10	13	17	225	5	7	9	12	15	20	25	250	3	4	6	8	10	14	18	250	5	7	9	13	16	21	27																

TABLE V

Probability (In Percent) of Developing Coronary Heart Disease in Eight Years According to Specified Characteristics.
Estimates Based on Data From the Puerto Rico Heart Health Program

Urban Man Aged 55 Years
(Average Risk is 6 Percent)

DOES NOT SMOKE CIGARETTES										SMOKES CIGARETTES									
SERUM CHOLESTEROL (MG/DL)	SYSTOLIC BLOOD PRESSURE (MM HG)								SERUM CHOLESTEROL (MG/DL)	SYSTOLIC BLOOD PRESSURE (MM HG)									
	105	120	135	150	165	180	195	105		120	135	150	165	180	195				
NO GLUCOSE INTOLERANCE	150	2	2	3	3	4	6	7	150	3	3	4	5	7	9	11			
	175	2	3	3	4	5	7	8	175	3	4	5	6	8	10	13			
	200	2	3	4	5	6	8	10	200	4	5	6	8	9	12	15			
	225	3	4	5	6	7	9	11	225	4	6	7	9	11	14	17			
	250	3	4	5	7	8	11	13	250	5	7	8	10	13	16	20			
	275	4	5	6	8	10	12	15	275	6	8	10	12	15	18	22			
SERUM CHOLESTEROL (MG/DL)	SYSTOLIC BLOOD PRESSURE (MM HG)								SERUM CHOLESTEROL (MG/DL)	SYSTOLIC BLOOD PRESSURE (MM HG)									
	105	120	135	150	165	180	195	105		120	135	150	165	180	195				
YES GLUCOSE INTOLERANCE	150	3	4	5	6	8	10	12	150	5	6	7	9	12	15	18			
	175	4	4	6	7	9	11	14	175	6	7	9	11	14	17	21			
	200	4	5	7	8	11	13	16	200	7	8	10	13	16	19	24			
	225	5	6	8	10	12	15	19	225	8	10	12	15	18	22	27			
	250	6	7	9	12	14	18	22	250	9	11	14	17	21	25	30			
	275	7	9	11	13	17	20	25	275	11	13	16	20	24	29	34			

TABLE VI
Probability (In Percent) of Developing Coronary Heart Disease in Eight Years According to Specified Characteristics.
Estimates Based on Data from the Puerto Rico Heart Health Program

Rural Man Aged 60 Years
(Average Risk is 6 Percent)

DOES NOT SMOKE CIGARETTES										SMOKES CIGARETTES									
	SERUM CHOLESTEROL		SYSTOLIC BLOOD PRESSURE (MM HG)					SERUM CHOLESTEROL		SYSTOLIC BLOOD PRESSURE (MM HG)									
	(MG/DL)		105	120	135	150	165	180	195	(MG/DL)		105	120	135	150	165	180	195	
NO GLUCOSE INTOLERANCE	150	2	3	4	5	7	9	12	150	3	5	6	8	11	14	18			
	175	2	3	4	5	7	10	13	175	4	5	7	9	12	15	19			
	200	2	3	4	6	8	10	13	200	4	5	7	9	12	16	21			
	225	3	3	5	6	8	11	14	225	4	6	7	10	13	17	22			
	250	3	4	5	7	9	11	15	250	4	6	8	10	14	18	23			
	275	3	4	5	7	9	12	16	275	5	6	8	11	15	19	24			
	SERUM CHOLESTEROL		SYSTOLIC BLOOD PRESSURE (MM HG)					SERUM CHOLESTEROL		SYSTOLIC BLOOD PRESSURE (MM HG)									
	(MG/DL)		105	120	135	150	165	180	195	(MG/DL)		105	120	135	150	165	180	195	
YES GLUCOSE INTOLERANCE	150	3	4	5	7	9	12	16	150	5	6	8	11	14	19	24			
	175	3	4	5	7	10	13	17	175	5	7	9	12	15	20	25			
	200	3	4	6	8	10	14	18	200	5	7	9	12	16	21	26			
	225	3	5	6	8	11	14	19	225	6	7	10	13	17	22	28			
	250	4	5	7	9	12	15	20	250	6	8	11	14	18	23	29			
	275	4	5	7	9	12	16	21	275	6	8	11	15	19	24	30			

TABLE VII

Probability (In Percent) of Developing Coronary Heart Disease in Eight Years According to Specified Characteristics.
Estimates Based on Data from the Puerto Rico Heart Health Program

Urban Man Aged 60 Years
(Average Risk is 7 Percent)

DOES NOT SMOKE CIGARETTES										SMOKES CIGARETTES									
	SERUM CHOLESTEROL (MG/DL)		SYSTOLIC BLOOD PRESSURE (MM HG)					SERUM CHOLESTEROL (MG/DL)		SYSTOLIC BLOOD PRESSURE (MM HG)									
	105	120	135	150	165	180	195	105	120	135	150	165	180	195					
NO GLUCOSE INTOLERANCE	150	2	2	3	4	5	6	8	150	3	4	5	6	8	10	12			
	175	2	3	4	5	6	7	9	175	4	4	6	7	9	11	14			
	200	3	3	4	5	7	9	11	200	4	5	7	8	11	13	16			
	225	3	4	5	6	8	10	13	225	5	6	8	10	12	15	19			
	250	4	5	6	8	9	12	15	250	6	7	9	12	14	18	22			
275	4	6	7	9	11	14	17	275	7	9	11	13	17	20	25				
YES GLUCOSE INTOLERANCE	150	3	4	5	7	9	11	13	150	5	7	8	10	13	16	20			
	175	4	5	6	8	10	13	16	175	6	8	10	12	15	19	23			
	200	5	6	8	9	12	15	18	200	7	9	11	14	18	21	26			
	225	6	7	9	11	14	17	21	225	9	11	13	16	20	25	29			
	250	7	8	10	13	16	20	24	250	10	13	15	19	23	28	33			
275	8	10	12	15	18	22	27	275	12	15	18	22	26	32	37				

felt they are generally representative of urban and rural areas. Risk probability tables compiled for other studies have been successful in predicting risk in groups of people other than those from which the tables were derived. Thus, the Framingham coronary risk probability tables have successfully estimated risk in groups of people with known risk in Chicago, Los Angeles, Tecumseh, Michigan, Minneapolis, and Albany (9).

The figures given in the tables should be viewed only as guides to risk, since they are based on only 5 risk factors. When evaluating risk, additional information needs to be considered. Thus, persons of low physical activity and those with certain electrocardiographic abnormalities (such as nonspecific ST and T wave changes, blocks, and left ventricular hypertrophy) may be at substantially greater risk than those who do not have these alterations.

These tables can be helpful not only in guiding the physician in handling cases at risk but also in the education and motivation of the patient to necessary management regimens.

At the present time, it has not been clearly demonstrated that adjusting risk factors to an acceptable level reduces the risk of CHD to that of a person who has always had acceptable risk factor levels. Nevertheless, it is likely that some reduction in risk does occur in adjusting risk factors. In persons with several abnormalities, the greatest improvement could be expected by the si-

multaneous correction of all present, rather than by adjustment of one or two only.

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BCG VERSUS ISONIAZID IN THE PREVENTION OF TUBERCULOSIS

José E. Sifontes, MD, FAAP

Summary: Presented in concise form are the results of the United States Public Health Service studies of BCG vaccination in Puerto Rico and tuberculosis isoniazid chemoprophylaxis carried out in the United States, Puerto Rico, México and Canada.

BCG prevented 8 cases of tuberculosis per 100,000 vaccinated per year. The study demonstrated that, even if the vaccine had been more effective, its impact would not have been significant since most of the cases of tuberculosis occurred among persons who could not be vaccinated because they had positive tuberculin reactions. On the other hand, it was in this group, as well as among contacts of tuberculosis cases, that isoniazid proved to be effective when compared with a placebo it effected reductions in tuberculosis morbidity of 71 percent to 88 percent during the treatment year and of 40 percent to 60 percent thereafter. Based upon these results, isoniazid was adopted in 1959 as the method of choice for prevention of tuberculosis in Puer-

to Rico. The subsequent results, in spite of imperfections in the method, have been satisfactory when measured in terms of reductions of infection, morbidity and mortality from tuberculosis in Puerto Rico.

Resumen: Se presentan en forma concisa los resultados de los estudios del Servicio de Salud Pública de los Estados Unidos sobre la vacunación con BCG en Puerto Rico y los de los estudios de la quimioprophilaxis de la tuberculosis con isoniácida realizados en los Estados Unidos, Puerto Rico, México y Canada.

La BCG evitó 8 casos de tuberculosis por 100,000 vacunados por año. El estudio demostró que, aunque la vacuna hubiese sido más eficaz, su efecto no habría sido importante ya que la mayoría de los casos de tuberculosis sucedió en personas que no se podían vacunar por tener una reacción positiva a la prueba de la tuberculina. Por otra parte, fue en este grupo y en los contactos de los enfermos tuberculosos que la isoniácida demostró su eficacia al compararse con un placebo: redujo la morbilidad por tuberculosis en cifras de 71 por ciento a 88 por ciento durante el año de tratamiento y entre 40 por ciento y 60 por ciento después de completado el mismo. Estos resultados sirvieron de base para que en Puerto Rico se adoptara la isoniácida como método de elección para la prevención de la tuberculosis desde el año 1959. Los resultados

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ulteriores, a pesar de las imperfecciones del método, han sido satisfactorios al medirse en términos de la reducción de la infección, morbilidad y mortalidad por tuberculosis en Puerto Rico.

Tuberculosis prevention can be accomplished by prompt and efficacious treatment of source cases, by vaccination of the non-infected with BCG and by isoniazid chemoprophylaxis.

The purpose of this paper is to compare the results of BCG vaccination with those of isoniazid prophylaxis in the prevention of tuberculosis. It is based upon cooperative studies sponsored by the United States Public Health Service. The author of this paper participated in various stages of the studies including planning, operations and evaluation. (1) (2) These studies were of such magnitude that large numbers of investigators had to participate. The duration of a follow-up, in some instances lasted almost a generation, and beyond the lifetime of two outstanding proponents and leaders of these efforts: Edith M. Lincoln and Carroll Palmer. Numerous papers have been published describing the results by Ferebee, Comstock, Mount, Edwards, and others. (3) (4) This paper will focus on some aspects of these trials that are relevant to Puerto Rico.

Materials and Methods

The BCG trials were carried out in Puerto Rico between 1949 and 1951. A vaccine prepared at the New York State Department of Health was utilized in a dose of 0.1 mg of BCG organisms given intracutaneously. Tuberculin tests done 6 to 13 months after vaccination showed that 93 percent of the

vaccinees became reactors to 10 TU dose of tuberculin. The participants included 160,241 children under the age of 18 who were divided into three groups: a group of 82,269 who could not be vaccinated because of positive reactions to tuberculin, a control group of 27,338 children who had negative tuberculin reactions and were not vaccinated, and a group of 50,634 vaccinated with BCG. The tuberculosis morbidity in all groups was recorded for 20 years. The decision about the validity of the diagnosis was made without knowing to which group the participant belonged.

There were over 68,000 participants of the isoniazid chemoprophylaxis trials from the U.S., Puerto Rico, Mexico and Canada. Different population groups were studied. These included children with primary infection, contacts of tuberculosis patients, inmates of institutions for mentally ill persons and Alaskan villagers. Participants were given bottles of medications containing either isoniazid or a placebo to be taken once daily for one year. The dose of isoniazid ranged between 5 and 10 mg/kg daily. The decision to remove a person from the study, because of tuberculosis and the decision as to whether the person had tuberculosis or not, were made without knowing whether the person had been receiving isoniazid or placebo. Participants were followed during the year of medication as well as 10 years or more thereafter, depending upon the group. The data herein presented was that available after six to eight years of follow-up. (5) Subsequent observations at 11 to 14 years did not alter the conclusions and demonstrated no evidence of increased isoniazid resistant strains due to its use as a chemoprophylactic agent. (6)

Results

BCG

The tuberculosis case rate per 100,000 persons per year, as shown in Table I, was 19.7 in the vaccinated group and 27.4 in the control group. The highest case rates were encountered among the persons who could not be vaccinated

TABLE I
Results of BCG Studies in Puerto Rico Initiated in 1948
Twenty-Year Follow Up

<i>Study Groups</i>	<i>Annual Tuberculosis case rate per 100,000</i>
<i>Positive Tuberculin Reactors</i>	
<i>Diameter of induration</i>	
<i>Over 15 mm</i>	160
<i>11 - 15 mm</i>	60
<i>Negative Tuberculin Non-Reactors</i>	
<i>Controls: not vaccinated</i>	27.4
<i>Vaccinated with BCG</i>	19.7

This table tells most of the story of BCG in Puerto Rico. It shows that over a period of 20 years, from 1949 to 1969, the highest incidence of tuberculosis occurred among those who could not benefit from BCG, the reactors to tuberculin. It demonstrates the low risk of developing tuberculosis among the non-reactors whether they were vaccinated or not. This was at a time when the annual risk of becoming infected with tuberculosis was over 1.6 percent (7). At present, this risk has diminished to around 0.2 percent per year so that by 1979 the risk of a non-reactor developing tuberculosis had diminished by at least 87 percent. This would make BCG even less useful today than it would have been at the time of this study. Furthermore, BCG would interfere with the interpretation of tuberculin reactions and the utilization of the tuberculin test for case finding, epidemiological studies and identification of candidates for isoniazid chemoprophylaxis.

because of positive tuberculin reactions. These were 60 for those with reactions 11 to 15 mm in diameter and 160 for those with reactions larger than 15 mm in diameter. These results indicated a modest protection afforded by BCG and were comparable to those reported by Frimodt-Moller in South India, Paul in Rhodesia, Levine and Sackett in New York City and Comstock and Webster in Muscogee County in Georgia. These results were in contrast with the high degree of effectiveness reported in other studies such as those performed by Aronson and Palmer in American Indians, Ferguson and Simes in Canadian Indians and newborns, Sargent et al in Algerian newborns, and the British Medical Research Council in British school-leavers. (4)

Irrespective of the degree of protection afforded by BCG, an important finding stood out. It was that the control group had low tuberculosis case rates. Even if a vaccine had been highly protective, this effect would not have translated itself into significant benefit in terms of morbidity in Puerto Rico. BCG vaccine in Puerto Rico prevented only 8 cases of tuberculosis per 100,000 vaccinated per year. It had no significant impact upon morbidity since most of the cases came from persons who could not have been vaccinated because they were already positive tuberculin reactors. These findings suggested that efforts should be directed toward the persons at greatest risk of becoming infected: the contacts of tuberculosis cases and those already infected as evidenced by positive tuberculin reactions. The isoniazid chemoprophylaxis trials were based upon this need.

Isoniazid Chemoprophylaxis Trials

The medication was discontinued by

a number of participants because of various side reactions ranging from gastrointestinal to non-specific. This could be most appropriately analyzed in the trials among contacts and Alaskan villagers in which approximately 17,000 persons took isoniazid and 17,000 took placebo. Three hundred and ninety five persons in the isoniazid group and 324 persons in the placebo group discontinued medications because of alleged side effects. The difference between the isoniazid and placebo group was of only 71 (0.4 percent) excess side reactions in the isoniazid group.

The percentage of persons who completed the year of medication was an important part of the study. It was found that, as a rule, between 74 and 86 percent of the participants of all the trials took the medications for the whole year.

In analyzing the results of the study, the persons who did not take the medication were included in the isoniazid group, since it was felt that in estimating the real impact of isoniazid chemoprophylaxis the human factor of non-compliance had to be accepted as reality. In spite of this the number of cases of tuberculosis in the placebo group was significantly larger than that of the isoniazid group. There were 196 cases of tuberculosis in the placebo group and 45 in the isoniazid group. The reduction in morbidity was 71 percent in the isoniazid group. After the treatment year, the differences between the isoniazid and placebo group persisted. There were 105 cases in the placebo group and 62 in the isoniazid group. A difference of 40 percent fewer cases in the isoniazid group. Isoniazid offered significant protection to contacts of tuberculosis patients as well as to infected persons, even when people who failed to take the medications were included in the computations for the respective groups. Among the contacts who took isonia-

zid 80 percent of the time for 10 months the reduction in morbidity was 88 percent during the treatment year and 60 percent during the subsequent 10 years of follow-up.

Discussion

Isoniazid is a highly effective though not perfect chemoprophylactic agent against tuberculosis. Its efficacy is enhanced by the fact that it benefits the group of people which is the potential source of most of the new tuberculosis cases. On the basis of these results, the Puerto Rico Health Department adopted isoniazid chemoprophylaxis instead of BCG as a method of tuberculosis control beginning in 1959. Isoniazid was administered to contacts of newly diagnosed cases of tuberculosis as well as to people with positive tuberculin reactions of all ages. Routine administration of isoniazid to those older than 35 years of age was interrupted in recent years when the risk of hepatitis in this age group became apparent. At present, isoniazid is recommended for those who have positive tuberculin reactions and are younger than 35 years of age, particularly, if they are in the pediatric age group. It is also advised for all who have evidence of tuberculin conversion from negative to positive within a year, those who have a positive tuberculin reaction and a doubtful pulmonary lesion or who have risk factors, which might produce activation of a tuberculous focus, (such as treatment with steroids, a gastrectomy, measles or measles vaccine, malignant disease and other factors that may be associated with T lymphocyte depression).

These recommendations have not been strictly enforced and all too often are ignored. Yet, isoniazid chemoprophylaxis plus therapy of the source cases, though carried out imper-

fectly, have coincided with decreases in the rates of infection, morbidity and mortality in Puerto Rico. Which factor has been predominant cannot be ascertained. Improvements in the standard of living, for example, may have played an additional important role. Regardless of which ingredient may be the most important one, it is a fact that tuberculous infection, morbidity and mortality have declined spectacularly in an island, which not too long ago had a tuberculosis problem comparable to that of the most severely affected countries in the world. The most reliable figures on infection rates involving comparable groups are those of medical students in whom there has been a decline in tuberculosis infection rates from 38 percent in 1964 to 5 percent in 1979. (7) Morbidity and mortality figures for the general population have been regularly available in Puerto Rico for most of the present century. (8) Between 1958 and 1978 the tuberculosis morbidity rate declined from 89 to 11 per 100,000. Between 1958 and 1977 the mortality from tuberculosis in Puerto Rico declined from 29 to 6 per 100,000. Most of the deaths from tuberculosis now occur in older people and most of the morbidity is also occurring in these age groups. The reliability of tuberculosis morbidity and mortality figures in Puerto Rico is a source of concern. The mycobacteriology services of the Puerto Rico Health Department have been, in recent years, extremely limited and this fact must be taken into consideration lest we become too optimistic. Tuberculosis is likely to continue as a persistent but declining problem through the year 2000. Tuberculosis cases will continue to arise from people who were infected before the decade of the 50's and these will in turn infect their contacts, particularly younger people. Fortunately, this problem can usually be identified and controlled. Formerly, we

had hundreds of children hospitalized with tuberculosis including tuberculous meningitis. (9) Now, at the University Children's Hospital, we see around one patient with tuberculous meningitis annually.

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CONTESTACIONES A MEDI-QUIZ

EVALUATION AND MANAGEMENT OF PLEURAL EFFUSIONS

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NEW ADVANCES IN THE IMMUNODIAGNOSIS OF PARASITIC INFECTIONS

II. COUNTERELECTROPHORESIS

George V. Hillyer, PhD and Irving G. Kagan, PhD

Summary: This is the second of a series of reviews on new advances in the immunodiagnosis of parasitic infections. Counterelectrophoresis is a sensitive qualitative precipitation test which is used widely for the serodiagnosis of parasitic infections. The available literature on its use is reviewed here.

Resumen: En el segundo de una serie de ensayos sobre nuevos adelantos en el inmunodiagnóstico de infecciones parasíticas se resume la literatura sobre el uso de una técnica de precipitación sensitiva y cualitativa conocida como contrainmunolectroforesis.

Introduction

In a previous report, we reviewed the literature on the use of the enzyme-linked immunosorbent assay for the serodiagnosis of parasitic infections (Hillyer and Kagan, 1979). We now report on the use of counter-

electrophoresis for the serodiagnosis of infections with animal parasites.

Counterelectrophoresis (Synonyms: one-dimensional double electroimmunodiffusion, countercurrent immunoelectrophoresis, counterimmunoelectrophoresis, electroprecipitation, electrosyneresis, immunoosmophoresis, immuno-electrodifffusion) is being used widely as an immunologic tool for the serodiagnosis of a wide variety of parasitic infections. In this test, the properties of buffers, supporting medium, and reactants are such that, in an electric current, antigen and antibody migrate in opposite directions simultaneously, so that they can meet, react, and precipitate somewhere between their respective origins. Thus, a requirement is that the antigens migrate toward the anode. Since the reactants migrate toward one another, results often may be obtained within 30 minutes or less. As in Ouchterlony immunodiffusion, the test is essentially qualitative although titrations may be performed to obtain rough estimates of antibody concentration. By placing parasite antigen in the cathodic well and patient serum in the anodic well, one can detect antibodies. Alternatively, by placing patient serum in the cathodic well and an appropriate antiparasite antiserum in the anodic well, one can measure circulating antigens.

Reviews on technical details and the

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TABLE I

Application of Counterelectrophoresis for the
Serodiagnosis of Infections with Parasitic Protozoa

Parasite	Detection	References
<i>Entamoeba histolytica</i>	<i>Antibodies in man</i>	<i>Sepúlveda et al, 1971</i> <i>Landa et al, 1972</i> <i>Krupp et al, 1974</i> <i>Farid et al, 1977</i> <i>Martuscelli et al, 1977</i> <i>Myjak, 1978</i> <i>Isibasi et al, 1978</i> <i>Bonilla et al, 1978</i> <i>Manweiller and Lederer, 1978</i> <i>Martuscelli et al, 1978</i> <i>Meerovitch et al, 1978</i> <i>Mithal and Mohapatra, 1978</i>
<i>Plasmodium falciparum</i> , <i>P. malariae</i>	<i>Antibodies in owl monkeys</i>	<i>Bidwell and Voller, 1975</i>
<i>Plasmodium berghei</i> , <i>P. vinckei</i>	<i>Antibodies and circulating antigens in mice and rats</i>	<i>Seitz, 1975</i>
<i>Leishmania donovani</i>	<i>Antibodies in man</i>	<i>Desowitz et al, 1975</i> <i>Rezai et al, 1977</i>
<i>Mucosal leishmaniasis</i>	<i>Antibodies in man</i>	<i>Abdalla, 1977</i>
<i>Trypanosoma cruzi</i>	<i>Antibodies in monkey</i>	<i>Desowitz et al, 1975</i>

application of counterelectrophoresis (CEP) for the serodiagnosis of parasitic infections have been published by Crowle (1973) and Draper (1976).

Protozoa

A summary of the literature reporting the use of CEP for the serodiagnosis of proto-

zoal infections is found in Table I.

Sepúlveda et al (1971) and Landa et al (1972) first used CEP for the diagnosis of human amebiasis. Krupp (1974) compared CEP with other serologic tests to evaluate sensitivity and aid in the interpretation of results with patients who had amebic liver abscess or amebic dysentery; she compared these with uninfected control persons of the same socioeconomic group. She found that the sensitivity and specificity of the CEP test compared favorably with indirect hemagglutination and was superior to immunodiffusion. None of the serologic tests, however, could differentiate antibodies present in an active infection from those persisting after treatment. Myjak et al (1978) used the test for diagnosing patients with dysenteric and extraintestinal amebiasis. Farid et al (1977) diagnosed by CEP nine additional cases of amebiasis which originally were classified as obscure fevers. However, Mannweiler and Lederer (1978) found a large number of false positive reactors among persons with no symptoms of amebiasis. Other applications of CEP for the diagnosis of amebiasis are listed in Table I. A commercial kit called "Amoebogen" is available from Hyland*, a Division of Travenol Laboratories, Inc.

Bidwell and Voller (1975) in a brief note reported the use of CEP to detect antibodies to *Plasmodium falciparum* and *P. malariae* in owl monkeys. They found that preliminary tests with sera from human malaria infections gave similar results. Seitz (1975) used the test in detecting malarial antigens or antibodies in the sera of rats and mice using cellulose acetate membranes, but development

of the reactions took at least 4 hours. Desowitz et al (1975), testing sera from human kala-azar or a monkeys with *T. cruzi* and promastigote forms as antigen, suggested that CEP may be of value for the serodiagnosis of infections with those parasites. Rezai et al (1977) found that CEP correlated with the indirect immunofluorescence test for the diagnosis of kala-azar and favored CEP, since it is "rapid and less sophisticated" for epidemiological surveys. Abdalla (1977) was also able to diagnose Sudan mucosal leishmaniasis by CEP but found no correlation between the number and strength of precipitin lines and immunofluorescent titer levels.

In summary, regarding the protozoa, the availability of a commercial kit for amebiasis makes CEP a useful tool for screening possible cases of amebiasis in endemic areas. The method is limited, however, because some workers have reported that using crude antigens may result in a large number of false positive reactors. Use of CEP for diagnosing other protozoal infections is still too preliminary for practical application.

Trematodes

Hillyer (1975) reported using CEP for the serodiagnosis of fascioliasis in rabbits, hamsters, mice rats, and humans utilizing extracts of *F. hepatica* adult worms. The crude antigen used, however, also reacted with many sera from humans with schistosomiasis mansoni, trichinosis, echinococcosis, cysticercosis, and amebiasis. The specificity of the test increased significantly with separation of the antigens by gel filtration (Hillyer and Capron, 1976; Santiago de Weil, 1976; Hillyer and Santiago de Weil, 1977). The test can detect fascioliasis as early as 2 weeks of

* Use of trade names is for identification only and does not constitute endorsement by the Public Health Service or by the U. S. Department of Health, Education, and Welfare.

TABLE II
Application of Counterelectrophoresis for the Serodiagnosis
Infections with Parasitic Trematodes

Parasite	Detection	References
<i>Fasciola hepatica</i>	<i>Antibodies in mice, rats, rabbits and man; prediction of chemotherapeutic success</i>	Hillyer, 1975 Hillyer and del Llano, 1976 Hillyer and Capron, 1976 Santiago de Weil and Hillyer, 1976 Hillyer and Santiago de Weil, 1977 Hillyer, 1978 Hillyer and Allain, 1979 Levine et al, 1980
	<i>Antibodies in ruminants</i>	Tiggele, 1978
<i>Schistosoma mansoni</i>	<i>Antibodies in man</i>	Scapin and Tendler, 1975 Scapin and Tendler, 1977
	<i>Antibodies and circulating antigens in baboons and man</i>	Phillips and Draper, 1975 Houba et al, 1976
<i>S. japonicum</i>	<i>Antibodies in man</i>	Hwu et al, 1978

infection (Hillyer and Santiago de Weil, unpublished; Levine et al, 1980) and has proven useful for the prediction of chemotherapeutic success in rabbits, mice and rats (Hillyer and del Llano de Díaz, 1976, Hillyer and Allain, 1979, Levine et al, 1980). Hillyer and Allain (1979) compared indirect hemagglutination and CEP for the serodiagnosis of fascioliasis and found CEP to be clearly superior. Levine et al (1980) found that CEP and the enzyme-

linked immunosorbent assay (ELISA) detected active *F. hepatica* infections earlier than parasitologic diagnosis by the Kato thick smear. CEP antibody levels, but not ELISA, diminished rapidly in rabbits treated after 26 weeks of infection.

Tiggele (1978) used CEP for the diagnosis of bovine fascioliasis but found the lines of precipitation difficult to read. He also observed that during the drying of the plates,

TABLE III

Application of Counterelectrophoresis for the Serodiagnosis of
Infections with Parasitic Cestodes and Nematodes

Group	Detection	References
Cestodes		
<i>Hydatid disease</i>	<i>Antibodies in man</i>	Kelkar and Kotwal, 1975 Pinon, 1976 Ardehali, et al 1977 De la Maza et al 1977 Todorov and Jeleva, 1979 Pinon et al 1979
<i>Taenia saginata</i>	<i>Antibodies in calves with cysticercosis</i>	Geerts and Kumar, 1977
<i>Taenia solium</i>	<i>Antibodies in humans with cysticercosis</i>	Desowitz et al 1977
Nematodes		
<i>Trichinella spiralis</i>	<i>Antibodies in man</i>	Despommier et al 1974
<i>Dirofilaria immitis</i>	<i>Antibodies in dogs and cat, and humans with bancroftian filariasis</i>	Desowitz and Una, 1976
	<i>Antibodies in dogs following therapy</i>	Desowitz et al 1978a
<i>Brugia pahangi</i>	<i>Antibodies in cats</i>	Desowitz et al 1978b

precipitation lines disappeared from the agar. This problem was corrected by pre-soaking the plates in a solution of zinc sulfate.

Phillips and Draper (1975) reported detecting circulating immune complexes in a considerable portion of individuals infected with *S. mansoni* by CEP although subsequently it was acknowledged that many of the anodal arcs of precipitation were due to artifacts (Draper, 1976). However, Houba et al (1976) using sera from monkeys with *S. mansoni*, found by CEP that worm gut-associated antigens appeared early in the infection, followed by membrane-associated antigens and, finally, soluble eggs antigens. Scapin and Tendler (1975) used adult worm antigens in CEP to detect antibodies in humans infected with *S. mansoni*. We have found this antigen to be unsatisfactory, however, due to the alarming number of false-negatives (Hillyer, unpublished). In a subsequent study Scapin and Tendler (1977) compared the use of KCL-extracted worm antigens with adult worm homogenates for the serodiagnosis of schistosomiasis, but correctly identified only 54 percent and 19 percent of the infected individuals. Hwu et al (1978) used a soluble egg antigen preparation and found that CEP was comparable to the circumoval precipitin test in detecting antibodies to *Schistosoma japonicum*. This study, however, needs to be confirmed by other investigators.

In Summary, CEP appears to be a viable serodiagnostic tool for detecting experimental infections of *F. hepatica* and for predicting the success of therapy. Further work is needed on cattle and sheep to determine its practicability with animals of economic importance. Improved specificity will require that pure antigens be available.

Cestodes and Nematodes

Pinon (1976) used CEP for the diag-

nosis of human hydatid disease. This was confirmed by Ardehali et al (1977) who, in addition, reported that human hydatid fluid was clearly superior to sheep hydatid fluid as antigen for diagnosing human infections. Todorov and Jeleva (1979) suggested that CEP be used as a screening test for mass case finding of human hydatid disease. Geerts and Kumar (1978) also used CEP for the diagnosis of bovine cysticercosis, with extracts of proglotides as antigen. Desowitz (1977) carried out an immunoepidemiological survey for cysticercosis in an endemic focus of Irian, Jaya (Indonesia) with CEP. All individuals with palpable subcutaneous cysticerci were serologically positive by this method, as were 77 percent of the individuals giving a history of epileptiform seizures. Also positive were 22.5 percent of the individuals with no clinical complaints.

As reported in our previous review (Hillyer and Kagan, 1979) Pinon and Dropsy (1977a,b) combined CEP with an enzyme immunoassay and termed this combination ELIEDA (enzyme-linked immunoelectrodiffusion assay). ELIEDA takes place in 3 steps: (1) CEP is carried out on a cellular acetate membrane; (2) the antigen-antibody precipitates are treated with peroxidase-labelled anti-immunoglobulin heavy chain; (3) the complexes are then demonstrated by the addition of the substrate. Since heavy chain specific antiserum is used, the type of immunoglobulin antibody involved in the test serum can be identified. Pinon et al (1979) compared CEP, ELIEDA, and immunoelectrophoresis (IEP) for the serodiagnosis of human hydatid disease. They used a specific human reference serum for hydatid arc 5 antigen. They found CEP more sensitive than IEP and ELIEDA slightly more sensitive than CEP. The authors considered ELIEDA complementary to CEP in that it determines specific classes of antibodies involved in the immune respon-

ses.

Despommier et al (1974) used cell-free homogenates of *T. spiralis* in their CEP test for the serodiagnosis of human trichinosis. The test was very accurate in diagnosing infected individuals, although cross-reactions were observed with some sera from patients with schistosomiasis or visceral larva migrans. Desowitz and Una (1973) used *Dirofilaria* antigens in counterelectrophoresis to detect infections in dogs and a cat infected with this parasite. Utilizing these same antigens they found that 17 of 24 humans living in a setting of hyperendemic subperiodic filariasis were positive with this test. Desowitz et al (1978) treated *D. immitis*-infected dogs with diethylcarbamazine and tested their serum periodically by CEP with various antigen preparations. In dogs showing severe to moderate adverse reactions to the drug, presumably due to the formation of immune complexes, decrease in antibody levels to a metabolic worm antigen was observed.

The potential of CEP in diagnosing infections with cestodes and nematodes requires further evaluation.

Concluding Comments

The U. S. National Library of Medicine "Medline" listed 283 articles as published during the last 3 years where counterelectrophoresis has been used. As can be seen from this review, CEP is a powerful tool for the serodiagnosis of a wide variety of experimental infection with parasites. Small amounts of reactants are required and, with the exception of power supply, the materials needed are inexpensive. The test is rapid in that one can often obtain a result in 1 hour or less, versus 24 hours or longer for other precipi-

tation tests. There are pitfalls, however, with this technique. Artifacts are often observed in the form of precipitate lines near the serum wells, particularly when crude antigens are used. Investigators need to determine optimum antigen concentrations, critical voltage or amperage output from the available power supplies, and optimum reaction times. The use of purified antigens will undoubtedly increase the immunologic specificity of the test.

Acknowledgments

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FLAVOBACTERIUM, INFECTIVE ENDOCARDITIS AND PROSTHETIC HEART VALVE

Charles D. Johnson, MD

Summary: I report a patient with *Flavobacterium*-induced infective endocarditis associated with a prosthetic mitral valve, who suffered central nervous system complications. The special characteristics and role of *Flavobacterium* in this context, and therapeutic dilemma presented, are emphasized.

Resumen: Se reporta sobre un paciente con endocarditis infecciosa inducida por *Flavobacterium* asociado con una válvula mitral prostética, quien sufrió complicaciones del sistema nervioso central. Las características especiales y el papel de *Flavobacterium* en este contexto, y el dilema terapéutico presentado, son enfatizados.

Infective endocarditis (IE) complicates prosthetic heart valves (PV) in 1-4 percent of patients, presenting a serious and difficult management problem (1-20). *Flavobacterium* is a rare etiology of IE and septicemia, particularly prosthetic valve endocarditis (PVE) (21-28). I wish to report a patient and review PVE due to *Flavobacterium*.

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Case Report

This 38-yr-old symptomatic male was initially evaluated in 1977 and diagnosed as having an atrial septal defect (ASD), mitral regurgitation (MR) and congestive heart failure. On September 14, 1977, he underwent open heart surgery, closure of the ASD (3 x 2.5 cm, foramen ovale type) with interrupted sutures and mitral valve replacement with a medium size Beall valve, model 106. Cephalothin, 1 g IV x 2 was administered on the first postoperative day. A fever of 38.5° C was present three days prior to surgery and 38.8° C postoperatively but this returned to normal. Preoperatively the Hb was 11 g, Hct 31 percent, leukocytes 12,700 and 6-12 white blood cells (WBC) were seen in the urine. The mitral valve was "wide open" and the valve leaflets thickened with retracted edges; the chordae tendineae of the septal leaflet were ruptured. Pathological examination showed thickening of the endocardium and focal myocardial fibrosis; there were cartilaginous-like fragments but no calcification; the mitral valve was fibrosed and hyalinized.

Later in 1977, he suffered atrial arrhythmias but had no fever; warfarin was continued. He continued to do well in 1978 (but with hematuria and pyuria) until early December, when he was admitted to the hospital with a dental abscess, a temperature of 38.1° on one occasion, anemia (8.9g and 7.8g of Mgh); leukocytosis, hematuria and pyuria. Dental extraction was performed. Benzathine penicillin and aqueous penicillin (400,00 u) were given three days prior to extraction. A total of 19 doses of aqueous penicillin was given in addition to an injection of streptomycin (1g) upon discharge. Afterwards, he felt well but the urine continued to show marked hematuria, pyuria, granular, red (RBC) and WBC

casts.

The patient was readmitted to the hospital on March 26, 1979 (age 40) because of fever (40°C), chills, headache, confusion, blurred vision, cough, incoherent speech and difficulty with recall, understanding and recognizing people, dysuria, clonus of the right foot, caries and poor oral hygiene. Laboratory data revealed a Hb of 8.3 g and the urine loaded with RBC's, many WBC's and casts. The cerebrospinal fluid (CSF) contained 132 mg of protein, glucose 50 mg percent, no organisms, 63 crenated RBC's and 152 WBC's- 70 percent polynuclear and 30 percent mononuclear. A throat culture grew *Klebsiella*, alpha hemolytic streptococcus, *Bacterium anitratum* and *Trichosporon*. The stool showed *Strongyloides* larvae. Blood cultures (5) drawn on the day of admission revealed *Flavobacterium*, sensitive to tetracycline and chloramphenicol but resistant to ampicillin, carbenicillin, cephalosporin, gentamicin, kanamycin, polymyxin B and tobramycin; penicillin was not tested. Repeated brain scans (radionuclide, gallium, computerized tomography) were compatible with brain infarcts, cerebritis, thrombotic process or abscesses in the left temporal and frontal lobes. Initially the patient received aqueous penicillin, gentamicin and chloramphenicol, which were altered on 4-5-79 to chloramphenicol 1 g IV q. 6 h x 4 d, then 500 mg q 6 h, and vancomycin 500 mg q 6 h IV, when the results of the blood cultures were received. Heparin, warfarin and later aspirin were variably administered, depending on different recommendations of consultants, but trying to maintain the prothrombin time (PT) in a low therapeutic range, when warfarin was given (until 4-5-79). Convulsions ensued on 4-4-79. An organic psychosis with restlessness, disorientation and hallucinations was prominent. Repeat urine and blood cultures were negative for bacteria and fungi except for one blood culture of 4-9-79, which was positive for *Pseudomonas* species. It was sensitive to erythromycin, gantrisin, penicillin, tetracycline, chloramphenicol, gentamicin, cephalosporin, carbenicillin and amikacin but resistant to ampicillin, streptomycin and kanamycin. A tachycardia of 132 was present on 4-14-79. He eventually improved clinically. Serial brain scans revealed complete resolution of the left hemispheric lesions. Chloram-

phenicol and vancomycin were discontinued after 44 days, and warfarin was restarted. The Hb was 10.8g. The discharge diagnoses were septic emboli producing temporal lobe, cerebral infarcts, and metabolic encephalopathy.

The patient became asymptomatic but the temperature was 38°C on one occasion, with mild leukocytosis, persistent hiccups and the urinalysis showing 1+ protein and 5-7 RBC's, while on warfarin. No overall changes ever occurred in the cardiopulmonary system.

Discussion

PVE occurs in 1-4 percent of patients with prosthetic valve surgery, 2-3 times more common, than after other open heart operations. The symptoms it presents are fever, chills, malaise, new murmurs, altered PV sounds, abnormal rocking of the valve on fluoroscopy, emboli (30-40 percent), positive blood cultures (often negative with fungi) and difficulty with eradication of infection. Valvular dysfunction may ensue as paravalvular leak and regurgitation, stenosis (mitral valve) or there may be no hemodynamic abnormality as in the patient presented. The process locates itself on suture lines with disruption and forms ring abscesses, being less common on the mitral than the aortic valve (1-20, 29).

Early PVE, within the first 2 months after the surgery, is due to *Staphylococcus epidermidis* and aureus, gram negative organisms, enterococci, diphtheroids and fungi (*Candida*, *Aspergillus*), organisms resistant to prophylactic antibiotics. It is related to surgical contamination and postoperative noncardiac bacteremia, and carries a high mortality of 60-88 percent. Late PVE, which is more common, occurs after 2 months, in 1 percent of operative patients per year, and is due to streptococci, especially viridans, and other organisms such as gram negatives, staphylococci, streptococcus faecalis

and fungi. These are similar to those causing IE in unoperated patients. It is probably related to predisposing episodes of transient bacteremia with dental, genitourinary (GU) and pyogenic skin infections, and carries a lesser mortality of 22-53 percent. It may present like typical native IE but an acute onset and rapid progressive course may follow with organisms other than streptococci (1-20, 30, 31).

Flavobacterium

The genus *Flavobacterium* are "water bugs or bacteria" composed of 3 main groups. *F. meningosepticum* (Group 1) was first isolated by King (32) in 1959. They are aerobic or facultative anaerobic, weakly fermentative, nonmotile, nonhemolytic, gram negative, slender slightly curved rods possessing positive catalase, oxidase and indol. However they show negative nitrate, citrate and variable urease reactions, as well as proteolytic activity against gelatin and litmus milk. It does not grow on enteric agar media and grows variably on MacConkey agar. It utilizes glucose in an open tube of OF medium. However, it grows on routine laboratory media such as blood agar at 37°C after incubation for 3-4 days. The colonies are convex, translucent and pigmented light to deep bright yellow, red or brown, or maybe a glistening grey-white color. It can be confused with nonpigmented strains of *Pseudomonas aeruginosa* (21, 22, 26, 27, 32-39). Unfortunately, in this case no further studies on the *Flavobacterium* were performed.

Flavobacterium was regarded as a nonpathogenic saprophyte widely distributed in water, soil, dairy products, the slime on putrefying meat, in lakes, ponds, river and sea but not part of the normal human bacterial flora. However, it has been isolated from the genitalia of asymptomatic subjects, pharynx of healthy neonates, the urine, sputum of debi-

litated patients and patients with a low immune status. It has been found in drinking and distilled water (water important in transmission), in surgical suite and hospital environment (equipment and antiseptic solutions) and is tolerant to chlorine (21, 22, 24-27, 33-36, 38, 40-42).

These microorganisms are opportunists causing nosocomial bacteremia in patients with indwelling arterial catheters (Group II) (28) and ICU pneumonia (43). They have been a noteworthy cause of neonatal meningitis as well as rare cases of meningitis and pneumonia in adults (32, 36-40, 43, 44). *Flavobacterium* has caused several cases of septicemia postoperatively but is a rare cause of IE per se (Table I) (21-28). The author is aware of only one previous case of *Flavobacterium*-induced PVE, Case 2 of Berry et al (22), a 37-yr-old male with rheumatic heart disease and a Starr-Edwards ball valve prosthesis, who was treated with chloramphenicol and enjoyed an uneventful course.

As in the patient presented, *Flavobacterium* demonstrated an antibiotic susceptibility pattern that is unique and identifying in that it is generally sensitive and responds to antibiotics that act primarily on gram positive organisms such as erythromycin, vancomycin, neomycin and perhaps chloramphenicol and rifamycin. It is extremely resistant to all potent aminoglycosides, polymyxins, cephalosporins and penicillins (one isolate was sensitive to ampicillin) (21, 23, 24, 27, 36, 38, 40, 43).

Neurological Complications

As observed in this patient, neuropsychiatric complications occur occasionally in PVE as well as in 10-50 percent of all patients with IE. Often they represent the chief complaint or a major presenting symptom (60 percent), and are a major source of morbidity

TABLE I

Flavobacterium Infective Endocarditis and Septicemia

Author Reference Year	Age / Sex	Diagnoses.	Symptoms.	Prophylaxis	Therapy	Outcome
Schiff et al (21) 1961	66 M Operator of fishing resort	Bacterial endocarditis. First reported case. ASHD, MI, SVT, AS. Acute pulmonary edema. Urinary tract infection, possible portal of entry, but urine culture negative. Fever, chills, etc. Numerous blood cultures positive. <i>S to novobiocin</i> . <i>R to most common antibiotics</i> .			chloramphenicol novobiocin sulfasoxizole. Various antibiotics and anticoagulants prior.	Myocardial abscess, necrosis. Died from rupture of mycotic aneurysm of AV cusp. Vegetation.
Berry et al (22) 1963		Septicemia. Cardiopulmonary bypass, OR source: heart-lung machine, water bath, floor. Systemic toxicity, lethargy.				All resolved promptly.
	7 M	Open intracardiac surgery. Repair of congenital MR. Fever. Prophylactic perioperative penicillin and streptomycin.			tetracycline streptomycin oxacillin	well
	37 M * Forester	RHD, MS, MR. Congestive heart failure. Starr-Edwards ball valve prosthesis. Fever. Penicillin and streptomycin.			chloramphenicol	Uneventful
	21 M Student	VSD closure. Increased CSF pressure. Chill, fever, seizure. Penicillin and streptomycin.			chloramphenicol tetracycline	well
	41 M Fire Chief	AS, commissurotomy. Penicillin and streptomycin, 6 days. Bright yellow, slender curved rod, not <i>F. meningosepticum</i> .				well
Pintér et al et al (23)	32 M Driver	Septicemia. Tooth extraction. Also Mima polymorphia. Septic fever, chills, leukocytosis; increased sedimentation rate. Splenomegaly, <i>S to neomycin</i> .			neomycin, unsuccessful. kanamycin	Flavobacterium disappeared from blood, but fever recurred. Fever subsided; recovered.

Olsen et al (24) 1965	32 to 68. 5 M's 3 F's 43 F	8 cases. Postoperative bacteremia and hyperpyrexia. <i>F. meningosepticum</i> . Hospital acquired, IV drugs, anesthesia air conditioning. Aortic, pulmonary, GI surgery, S to erythromycin, vancomycin, novobiocin. Valvotomy or MS	penicillin streptomycin	Mild course. All recovered rapidly without sequela from infection.
Olsen (25)		10 cases. Postoperative infection.		
DuPont, Spink (26) 1969	4 month to 78 yr.	20 patients. Bacteremia. Questionable contaminated water in OR, IV solutions, drugs. Receiving myelosuppressive therapy; 4 on antibiotics prior; 2 meningitis; 2 followed urinary catheterization; 7 occurred shortly after major surgical procedure; 2 developed shock.		3 deaths.
	8 F	3 post-cardiac surgery: Organism in multiple blood specimens. Antibiotics prior.		Rec
	19 M	Antibiotic prior.		Rec
	31 M			Died
Werthamer et al (27) 1972	30 M Mexican	Subacute bacterial endocarditis. History of RHD. Drug addict. <i>F. meningosepticum</i> , type F; numerous blood cultures positive over 30 days. Chills, fever. S to chloramphenicol, erythromycin and vancomycin.	Surgery chloramphenicol erythromycin Intermittent gentamicin and carbenicillin.	Afebrile and negative blood cultures after surgery.
Stamm et al (28) 1975		14 patients, 49 blood cultures. Outbreak of Nosocomial Bacteremia secondary to indwelling arterial catheters (monitoring blood gases). From ice in ice machine in ICU. Leukocytosis.	Prompt appropriate antibiotic therapy.	No deaths directly attributable to <i>Flavobacterium</i> .

Abbreviations: AS = aortic stenosis; ASHD = atherosclerotic heart disease; AV = aortic valve; CSF = cerebrospinal fluid; GI = gastrointestinal; IV = intravenous; MI = myocardial infarction, MR = mitral regurgitation; MS = mitral stenosis; OR = operating room; R = resistant; Rec = recovered; RHD = rheumatic heart disease; S = sensitive; SVT = supraventricular tachycardia; * = see text.

and mortality (50 percent). Cerebrovascular lesions are most common (50 percent). Infected cerebral emboli occur in 6-31 percent of patients and can explain cerebral mycotic aneurysms (rupture, fatal) (2-10 percent of cases; usually the middle cerebral artery), cerebral infarcts and cerebritis, cerebral and subarachnoid hemorrhages (second commonest cause of death in IE), abscess (1 percent), stroke (55 percent)- hemiplegia, sensory and motor aphasia, etc. Toxic encephalopathy, convulsions and organic psychoses (hallucinations, fluctuating delirium, disorientation, paranoid ideation) are frequent (60 percent), explained by infarct or hemorrhage (1, 2, 7, 17, 19, 45-48).

Prevention

Frequent and thorough cleansing and sterilization should be practiced in the hospital to avoid growth favoring conditions for *Flavobacterium*. Preoperative dental and GU care, probably perioperative antibiotics, especially for those undergoing PV replacement and control of surgical factors (contamination, operative time, use of nonporous suture material) should be practiced. Patients with PV's undergoing dental, GU, gastrointestinal and other procedures deserve prophylactic antibiotics (1, 2, 30, 31, 35, 40, 41, 49). The relative susceptibility to IE of tissue valves compared to rigid prostheses is controversial (17, 49, 50).

Therapy

PVE should be treated early and aggressively for 4-8 weeks with large dosages of appropriate bactericidal parenteral antibiotics,

often in combinations. This can be done in referral centers where consultations in infectious disease, nephrology, cardiology and cardiovascular surgery are immediately available (17). *Flavobacterium* infections have responded to chloramphenicol, vancomycin and erythromycin. Early valvular replacement, plus antibiotics may be indicated for congestive heart failure, emboli, a new regurgitant murmur, atrioventricular conduction disturbances, nonstreptococcal and fungal endocarditis, myocardial invasion with persistent infection and fever, PV dysfunction and relapse after antibiotic therapy (1-3, 5-8, 10-19, 51). For neurological complications bactericidal drugs are necessary; mannitol, urea and steroids may alleviate cerebral edema. Neurosurgery should be considered for cerebral abscesses, hematoma, mycotic aneurysms and emergency decompression (48).

Anticoagulants

Data for the withholding or administration of anticoagulants in PVE is not yet available. In the past they have been considered generally contraindicated for fear of CNS hemorrhage in the presence of an embolic vegetation. Johnson (11) recommends their discontinuation. Major cerebral emboli with hemorrhage was the second commonest cause of his deaths, seen in 50 percent of autopsy patients, all on anticoagulants. Similarly, Karchmer (2) observed 12 of 42 (28 percent) patients on anticoagulants suffered CNS events; 5 with late onset PVE suffered massive intracerebral hemorrhage or hemorrhagic infarcts; the PT was $> 2 \times$ normal in 3 of the 5. Others (52, 53) have also observed similar complications. While recognizing the dangers of anticoagulants, it is appreciated that they do decrease emboli and should be considered in patients with life-

threatening thromboemboli (48, 52-54). Bloch and Lieberman (52, 53) would stop them once nonhemorrhagic or hemorrhagic infarcts have occurred. But discontinuation may not necessarily be imperative (Lerner, Weinstein) (45), as morbidity and mortality may not be augmented, and CNS and systemic emboli may ensue if anticoagulation is inadequate or stopped. Wilson (45) et al (53) found CNS complications to be 9 times more frequent if anticoagulants were stopped (58 percent CNS symptoms) with a higher mortality, than in those taking these agents (8 percent CNS symptoms). At autopsy CNS complications were regarded as the primary cause of 5 of his 8 deaths (3 of the 5 had massive intracerebral bleeding due to thromboembolism) without adequate anticoagulation and only one death was due to anticoagulants. Many maintain the PT at a lower therapeutic range, about 1 1/1 x control (2, 52). Wilson (45) suggests a prudent course as follows: If CNS complications occur anticoagulants may be temporarily discontinued, observing for clinical and laboratory evidence of intracranial bleeding (a CAT scan may be useful at this point); if none occurs reinstate them preferably within 48-72 hours. The PT may not be in therapeutic range but is sufficient to prevent valve thrombogenesis until they are resumed, as CNS complications were delayed 7-23 days after their discontinuation. Angiography is indicated for a suspected ruptured cerebral aneurysm and anticoagulants are withheld several days for any surgical evacuation of blood clot (2, 16, 45, 53).

Flavobacterium Associated with a Prosthetic Mitral Valve

The source of the *Flavobacterium* in this patient is unknown; acquisition at the time

of surgery or during the GU and dental infections with extraction are suspicious. It is of interest that *Trichosporon* (a yeast related to *Candida*, recovered from the mouth, cause of brain abscess and endocarditis of heart valves and prosthetic devices) (34, 55) and *B. anitratum* (*Acinetobacter*, which has been isolated from the blood - septicemia and subacute bacterial endocarditis - urine, CSF, sputum, in and on the human body) were recovered from his throat culture. These latter organisms and *Flavobacterium* must be distinguished from *Pseudomonas aeruginosa* (34, 39, 56).

The association of secundum ASD and MR, as present in this patient, has been increasingly recognized (57,58).

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PEDIATRIA, EL PATITO FEO

De todas las especialidades médicas, Medicina Interna y Cirugía, siempre han tenido un sitio preferencial. Obstetricia y Ginecología, también ha ocupado un sitio preferencial probablemente por la atracción especial que ejerce el sexo, la fecundación y el desarrollo maravilloso de un nuevo ser. Pediatría, sin embargo, en general ha sido relegada a un segundo plano y muchas veces ni siquiera considerada como especialidad.

Es posible que algunos me acusen de estar prejuiciado y otros de acomplejado por lo que acabo de expresar. Sin embargo, los que me conocen saben que practico la medicina enamorado de mi especialidad. Para los que crean que soy un acomplejado, quiero ofrecer una justificación personal o mejor una explicación racional. El internista, es visto por la mayoría como el médico que trata las enfermedades más importantes que ocupan los volúmenes más extensos de los textos de medicina. El cirujano es el que resuelve en el quirófano con su varita mágica llamada bisturí, lo que no se ha podido solucionar médicamente ... y el obstetra, por otro acto cuasi-mágico “produce” un bebé, en el que 15 o 20 por ciento de los casos son por operación cesárea. Al pediatra, sin embargo, a menudo lo pintan como un médico general de niños, más que un verdadero especialista. Entréguele, sin embargo, un infante a un médico general o a un internista y comprobará, sin lugar a dudas, que la pediatría es una verdadera especialidad que requiere una clase especial de médico.

Todo esto que estoy expresando medio en broma y medio en serio, ha vuelto a adquirir relevancia ahora que ha terminado el Año Internacional del Niño. Me refiero a la actitud de relego para los niños y la pediatría. Esta actitud de indiferencia y relego que he podido observar a lo largo de mi carrera profesional desde la escuela de medicina y a través de mi internado, residencia, servicio militar, programas gubernamentales a nivel municipal o estatal y hospitales privados, todavía existe. Menos que antes, pero todavía existe. Ya, por lo menos, se reconoce la importancia de un cardiólogo pediátrico o de un nefrólogo pediátrico o de un neurólogo pediátrico. Hasta contamos con cirujanos pediátricos, gastroenterólogos pediátricos y ginecólogos pediátricos. La neonatología ha sido la confirmación de nuestra especialidad, si es que alguien llegó a dudarlo.

*Sin embargo, que trabajo ha costado conseguir un Hospital de Niños para **cuidado primario**. Al poco tiempo, su departamento de cuidado intensivo ha resultado ser insuficiente para la demanda tan grande de servicios especializados. ¿Que trabajo cuesta establecer un departamento organizado de toxicología o de conseguir un neurocirujano para resolver un caso de un hematoma subdural! De las facilidades para niños retardados ni siquiera quiero hablar.*

En práctica privada, el cuadro dá ganas de llorar. Hay hospitales privados que ofreciendo servicios obstétricos hasta hace poco, no tenían un nursery. Algunos todavía, no tienen un departamento de pediatría y los que lo tienen son tan limitados en sus servicios que no merecen ni siquiera llamarse Departamento de Pediatría. Las secciones de aislamiento y/o gastroenteritis tan frecuente en pediatría, brillan por su ausencia o deficiencia. La necesidad de un hospital de niños en la comunidad para que los pediatras del área metropolitana puedan dar un servicio comprensivo y de

calidad, es primordial. Es posible, que algunos oficiales o médicos de agencias gubernamentales o privadas, consideren que el número de cunas o camas pediátricas en la comunidad sea suficiente. Esto resulta debatible. Pero aún cuando fuera cierto, lo que en realidad agrave el problema es que ese número limitado de cunas o camas pediátricas esté desparramado entre tantos hospitales privados haciendo más difícil la contratación del personal de enfermería especializado y la prestación de unos servicios más globales y completos a nuestra población infantil. El que tenga dudas sobre la falta que hace un **"Hospital Pediátrico de la Comunidad"** que se lo pregunte a cualquier pediatra en práctica. El problema estriba en quien es el valiente que le pone el cascabel al gato.

Quiero también manifestar la honda satisfacción del empuje que ha recibido la medicina preventiva durante el año 1979 con la intensificación de los programas de vacunación a todos los niveles, tanto privados como gubernamentales. Un factor importante ha sido la implementación de la ley que exige a todos los niños de edad escolar que estén debidamente vacunados.

Por último, el adelanto más grande del Año Internacional del Niño es probablemente el despertar de las conciencias de los líderes de la empresa privada y gubernamental para que aunen esfuerzos en pro del mejoramiento de la salud física y mental de los niños sanos e impedidos de Puerto Rico. Mientras tanto, yo continúo con el sueño dorado del día en que **El Patito Feo** se convierta en un cisne esplendoroso y completamente desarrollado.

Eduardo Vachier, MD
Pasado-Presidente Sección de Pediatría
Asociación Médica de Puerto Rico

GLUCAGON EN GASTROENTEROLOGIA

Ed. José Picazo, MD, Tela, Inglés.
MTP Press Ltd. Falcon House
Lancaster, Inglaterra, 1979

El glucagón, hormona alfa pancreática, antagonista de la insulina, hasta hace aproximadamente dos décadas había revestido poco interés, a excepción de su efecto hiperglicemiante. En años recientes su utilidad terapéutica en gastroenterología y ramas asociadas, al igual que su utilidad diagnóstica, han sido ampliamente estudiadas.

El 31 de mayo de 1978, la Facultad de Medicina de la Universidad Complutense de Madrid sirvió de sede a una mesa de trabajo internacional donde prominentes figuras mundiales discutieron ampliamente las virtudes y aplicaciones de la hormona en los campos de la fisiología, radiología, endoscopia, cirugía y hepatología. De la interrelación disciplinaria surgieron nuevos puntos de vista, ideas y aplicaciones para un futuro.

El Dr. José Picazo, editor, al igual que el Dr. A. Oriol Bosch, Decano de la Facultad de Medicina de la Universidad Complutense de Madrid, quien presidiera el simposio, le extendemos nuestras felicitaciones por tan excelente recopilación de los trabajos presentados y a la editorial MTP Ltd. de Inglaterra por la gran calidad del libro. Consideramos la obra excelente libro para el lector interesado en el tema.

El primer capítulo, por los doctores A. Gómez-Pan, G. Blesa-Malpica, Rodríguez Arnao y A. Oriol-Bosch, de España, discute ampliamente las acciones y utilidad medicamentosa del glucagón sobre la secreción de hor-

monas de crecimiento, secreción de catecolaminas, en pruebas funcionales hepáticas sobre la secreción gástrica, la contractilidad cardíaca, como hormona hiperglicemiante y en pruebas de secreción insulínica.

En el segundo capítulo, los doctores D. L. Wingate y E. Pearse, de Inglaterra, describen sus estudios de la fisiología del glucagón en el conducto gastrointestinal, mostrando sus efectos estimuladores de la actividad motora cuando se administra en forma continua.

Los capítulos tercero (Dr. J. Myren, Noruega), cuarto (Dr. B. Ek, Suecia), y quinto (Dr. L. Kreel, Inglaterra) muestran su utilidad en estudios diagnósticos endoscópicos, colonoscópicos y radiológicos, respectivamente. Su excelencia como agente de premedicación para estos procedimientos queda demostrado, favoreciendo la disminución del tono y la contractilidad gastrointestinal durante los estudios realizados.

Los capítulos sexto (Dres. M. J. Treffot, F. Quilichini y M. F. Vinson, Francia), séptimo (Dr. J. D. McCarthy, Estados Unidos) y octavo (Dr. F. Paul, Alemania Occidental) tratan de su utilidad en estudios diagnósticos, cirugía y manejo de anomalías biliares. Su utilidad en estudios gastrointestinales diversos, desde prueba simple de bario hasta arteriografía, tomografía computerizada y radiomanometría biliar, queda ampliamente demostrada. Sus efectos coleréticos y espasmolíticos resultaron efectivos en el

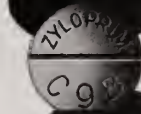
tratamiento de cólicos biliares. El capítulo nueve (Dr. N. A. Volpi-Celli, Estados Unidos) contiene interesantes sugerencias como factor hepatoprotector el efecto hepatotrófico de la insulina y el glucagón. Completan la obra dis-

cusiones, y preguntas y respuestas de los participantes al final de cada capítulo.

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ALTERNATIVE APPROACH TO THE MANAGEMENT OF MYOCARDIAL ISCHEMIA

Although coronary artery spasm has long been suspected to play an important role in the pathophysiology of myocardial ischemia (1), it has been held for many years that angina pectoris and myocardial infarction result from coronary atherosclerosis with or without superimposed coronary thrombosis. However, in the late 1950's the theory of vasospasm was revived and a specific syndrome characterized by chest pain at rest and marked ST segment elevations on the electrocardiogram was tentatively attributed to episodes of sustained coronary constriction (2).

Subsequently, coronary vasospasm was implicated in other anginal syndromes. For instance, patients presenting with unstable angina with or without progression to myocardial infarction may suffer from coronary angiospastic disease (3, 4). Furthermore, there is increasing evidence indicating that coronary vasospasm may trigger exercise-related episodes of myocardial ischemia (5). Therefore, classical exertional angina, unstable angina, and vasospastic angina may not be readily distinguished on clinical grounds, and there is some question to which extent these anginal syndromes represent distinct pathophysiological entities.

*Clinical experience has shown that conventional anti-anginal regimens including nitrates and β -adrenergic blockade may be ineffective in relieving coronary vasospasm. In fact, it has been claimed that β -blockers may aggravate ischemia caused by coronary spasm (6). The search for new coronary dilators during the 1960's led to the development of potent vasodilators which were subsequently classified as Ca^{2+} - antagonists (7). Shortly after their introduction, some of these new vasodilators were noted to be effective in the treatment of rest angina associated with coronary vasospasm. The potent spasmolytic activity of these agents was attributed to an inhibition of the inward movement of Ca^{2+} into smooth muscle cells (8). Among the many compounds with Ca^{2+} - antagonistic properties, nifedipine, verapamil, and diltiazem have received the most attention. **In vitro**, these vasodilators have been found to inhibit myocardial contractility in low concentrations, a property that distinguishes them from the conventional vasodilators such as nitroglycerin or papaverine. However, in the intact organism the action of these agents appear to be dominated by their vasodilator effects (9). However, despite this common denominator, drugs such as verapamil, nifedipine, and diltiazem may differ considerably in their pharmacological activity. The pharmacology of verapamil has proved to be complex. The optical isomers of this drug exert disparate electrophysiological effects. Thus, the Ca^{2+} -antagonistic activity has been attributed to the (-) isomer, whereas the (+) isomer appears to act predominantly as a local anesthetic (10). These unique electrophysiological properties may partly account for the anti-arrhythmic activity of the drug (11).*

On the other hand, nifedipine acts predominantly as a coronary and systemic vasodilator and is of little value as an anti-arrhythmic agent (12). Nifedipine has been reported to alleviate vasospastic angina in 90 percent of the patients (13). Similar results have been obtained with diltiazem, another agent with Ca^{2+} -antagonistic properties (13). Thus, there is little doubt that these agents provide a valuable therapeutic tool for the treatment of coronary spasm. It remains to be seen, however, whether these vasodilators are comparably efficacious in the treatment of conventional anginal syndromes.

Previous experiments from our laboratory have demonstrated that nifedipine exerts protective effects on ischemic myocardium. Those agents retard the development of ischemic contraction and inhibit the accumulation of intracellular Ca^{2+} in isolated hearts subjected to global ischemia (14). Furthermore, nifedipine protects the globally ischemic canine heart during cardiopulmonary bypass. Ischemic injury of the bypassed heart is reduced and its mechanical recovery after reperfusion is improved (15). In addition, studies on experimental infarction in dogs have revealed that nifedipine may enhance collateral flow and reduce permanent injury (16). Of considerable interest is the observation that treatment with nifedipine preserves local contractility in ischemic myocardium, suggesting that protection does not occur at the expense of the performance of the myocardium at risk (17). Recent clinical studies suggest that nifedipine may augment coronary flow to the underperfused myocardium in man (18).

Clinical and experimental studies thus support the view that Ca^{2+} -antagonists are useful for the treatment of myocardial ischemia in man. Although the mode of action of these drugs is not yet completely understood, one may assume that beneficial effects result from several actions. The drugs augment coronary flow and at the same time unload the ventricles by reducing peripheral impedance. In addition, they may exert direct effects on ischemic myocardial cells. In combination, these actions may explain the potent effects of Ca^{2+} -antagonists on the ischemic heart. Ongoing clinical trials should help further to delineate the value of Ca^{2+} -antagonistic vasodilators for the management of patients with myocardial ischemia.

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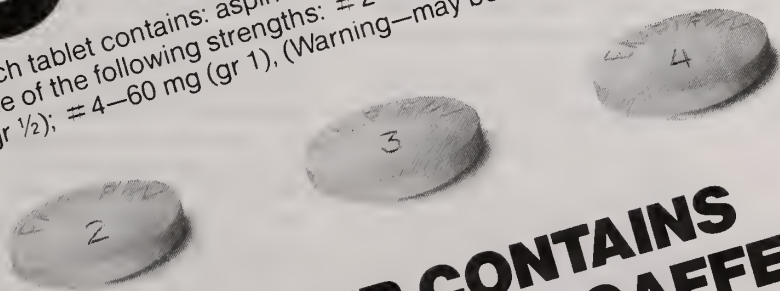
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Bursitis Brings Pain in Joints

Bursitis Brings Pain

Sometimes it's "housemaids knee." Or "policeman's heel."

By any other name it's still bursitis. It is one of mankind's more painful and disabling ailments.

Bursitis, says the American Medical Association, means inflammation of a lubricating sac about a joint. The sac, called a bursa, is similar to a collapsed balloon with some fluid inside. It is located at various places in the body where joints or tissues touch and rub. Without cushioning there would be friction.

Bursitis can hit many points in the body, but most often occurs in the shoulder, elbow or knee.

In almost every case bursitis follows unaccustomed strain or overuse of a limb. By taking a little time to warm up to your physical condition, and espe-

cially by training the muscles that you plan to use in any repetitious motion outside your normal activity (strengthening your wrist and arm before starting to paint the house, for instance) you can probably keep clear of this common and painful ailment.

If you get bursitis, no one need suggest that you see a doctor. The pain is so acute that you will be the first to seek relief.

There is much your doctor can do to relieve the pain and promote healing. One of the mainstays in treatment is a mild pain killer. Cortisone-type drugs have been used with some success. Heat treatments also have their place in bursitis therapy. In extreme cases, surgery may be required.

The basic treatment is complete rest in bed. Anything that will lessen the chance of the afflicted joint being moved will ease the pain and speed healing.

Like bearings in mechanical things, your bursa stay trouble-free much longer if you warm up slowly and let them get fully lubricated before you race the motor.



August, 1979
Frank Chappell
Science News Editor
AMA

EVALUATION AND MANAGEMENT OF PLEURAL EFFUSIONS

In normal circumstances, transudation of fluid into the pleural space and its re-absorption occur according to Starlings law. This establishes that the flow of fluid across the semi-permeable membrane depends on the difference of hydrostatic and oncotic pressures on both sides of the membrane.

Pleural lymphatics may play a crucial role in the re-absorption of fluids from pleural space, specially in conditions that limit the passage of pleural fluid towards pulmonary capillaries. Pleural effusions may be due to increases in capillary permeability like is seen in inflammatory or neoplastic processes, increases in the hydrostatic pressure of the pulmonary capillary as is seen in congestive heart failure, and diminution in the capillary oncotic pressure like in hypoalbuminemia and as a result of processes that interfere with the lymphatic drainage of the pleural space such as certain infections, tumors, trauma and some diaphragmatic processes. The typical X-ray appearance of a pleural effusion is characterized by the presence of the meniscus sign. Subpulmonic effusions and phantom tumors are examples of atypical radiologic presentation of pleural effusions.

Pleural fluid is considered to be a transudate if the total protein content is less than 3 gram per d/l and an exudate if greater than 3 grams per d/l. This separation can be made with greater precision if simultaneous measurements of the levels of protein and lactic dehydrogenase are measured in the patient's serum as well as in the pleural fluid.

The most frequent causes of transudates are: congestive heart failure, nephrosis and cirrhosis with hypoalbuminemia; exudates are usually due to inflammatory infectious or malignants processes.

The pleural fluid should be sent for cytology, glucose, amylase cell count, differential and cultures.

In some cases the pH of the pleural fluid may be useful in deciding whether a pleural fluid will require chest tube drainage for its management. Either pleural biopsies or those performed through a small thoracotomy incision may be very helpful in the diagnostic evaluation of pleural processes. An empyema is characterized by the presence of pus in the pleural space and its management should include chest tube drainage and appropriate antibiotics.

1. Pleural effusions due to congestive heart failure are usually due to:
 - a. An increase in the pulmonary capillary hydrostatic pressure
 - b. Increases in capillary permeability
 - c. Pleural inflammation
 - d. All of the above.
2. Tuberculous pleuresy:
 - a. Occurs up to 80 percent of the cases with primary tuberculosis
 - b. Positive cultures for *M. tuberculosis* can be obtained in approximately 30 percent of the cases.
 - c. Is characterized by a very high number of mesothelial cells
 - d. Frequently occurs in patients with persistently negative tuberculin tests.
3. The level of glucose in pleural fluid may be diminished in:
 - a. Malignant mesothelioma
 - b. Rheumatoid arthritis
 - c. Bacterial infections
 - d. All of the above.
4. Pancreatitis must be suspected as a cause of pleural effusion when:
 - a. The amylase concentration in the pleural fluid is less than that of plasma
 - b. The concentration of amylase in the pleural fluid is greater than that in plasma
 - c. The concentration of amylase in the plasma is equal to that of the pleural fluid.
 - d. All of the above .
5. In parapneumonic effusions, a pH of the pleural fluid below 7.2:
 - a. Indicates that the patient must be treated with antibiotics exclusively

- b. That the patient must be treated with antibiotics and with chest tube drainage of the effusion.
 - c. That the patient is acidotic
 - d. That intravenous bicarbonate must be administered.
6. The following statements can be made in relation to primary tumors of the pleura:
- a. Localized fibrous mesothelioma is a malignant disease that should be aggressively treated with chemotherapy.
 - b. The diffuse pleural mesothelioma has a favorable prognosis if it is treated with radiotherapy or chemotherapy
 - c. The diffuse mesothelioma is a benign tumor that may be associated in some cases with asbestosis
 - d. The localized fibrous mesothelioma may produce hypertrophic pulmonary osteoarthropaty
7. Pleural effusions associated to congestive heart failure:
- a. Are always exudates
 - b. Are always transudates
 - c. Are usually exudates but when the effusion is chronic may be transudates
 - d. Are usually transudates but when the effusion is chronic may become exudates.
8. Between 80 and 90 percent of the fluid filtered towards the pleural space:
- a. Is reabsorbed through the pulmonary lymphatics
 - b. Is reabsorbed in the venous side of the pulmonary capillaries
 - c. Is reabsorbed in the capillaries adjacent to the parietal pleura
 - d. Usually stays in the pleural space

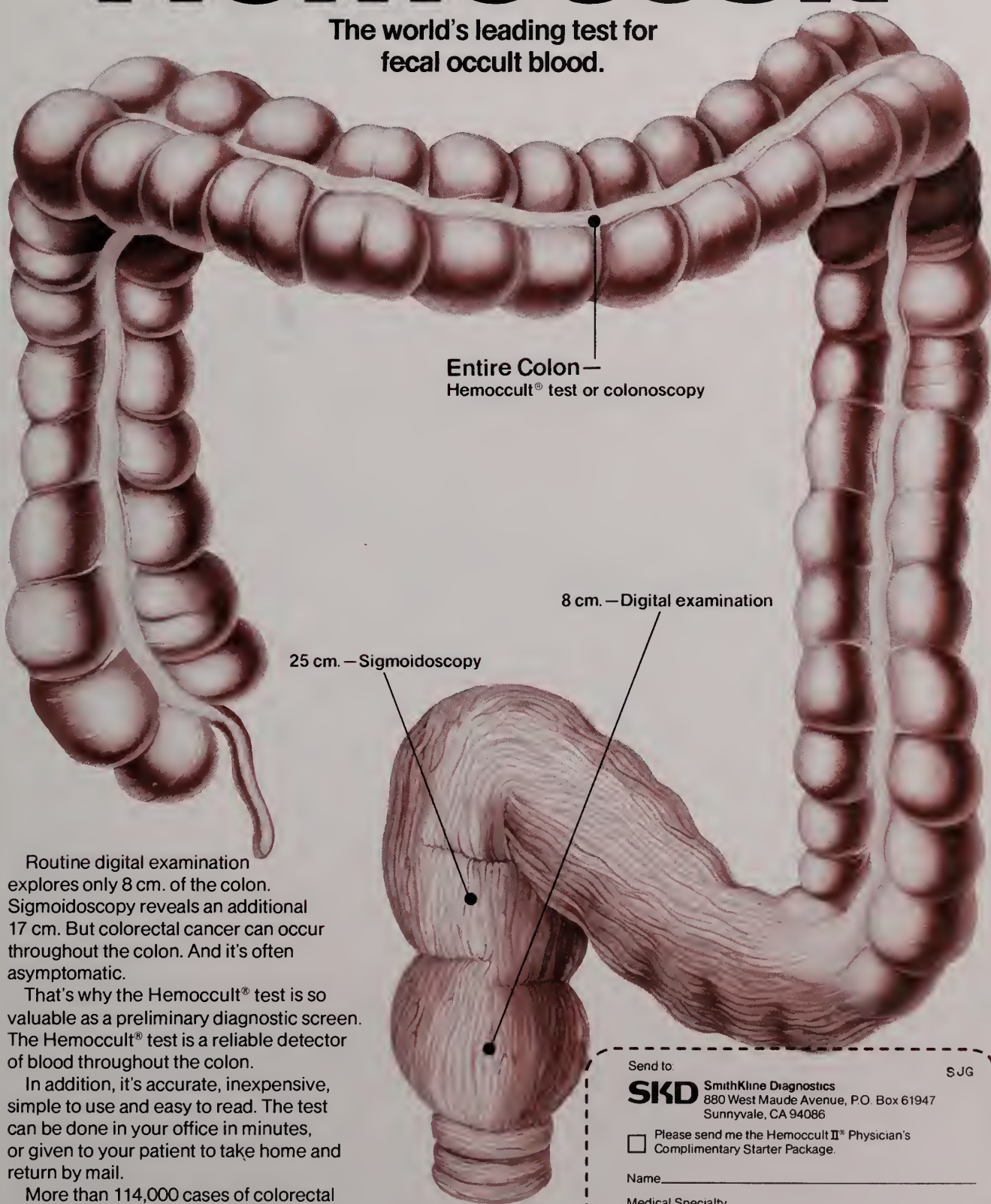
9. Conditions where the oncotic pressure of plasma is markedly reduced may cause:
- a. An increase in the amount of liquid that is filtered from the capillaries of the parietal pleura
 - b. A diminution in the reabsorption of fluid by the visceral pleural capillaries
 - c. An increase in the reabsorption of fluid by the lymphatic system
 - d. All of the above.
10. Malignant pleural effusions may be caused by:
- a. An increase in the permeability of the capillaries supplying the tumor
 - b. Lymphatic obstruction
 - c. By direct invasion of the pleura
 - d. All of the above.

Submitted by Arturo Córdoba, MD
Chief, Pneumology Section VAH

(Contestaciones en página 116)

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**When painful spasm
is the presenting
symptom...**



...in the functional bowel/irritable bowel syndrome*

Bentyl[®]

(dicyclomine hydrochloride USP)

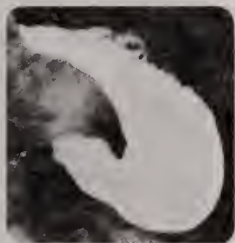
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10 mg./5 ml. syrup, 10 mg./ml. injection

helps control abnormal motor activity
with minimal anticholinergic side effects†

Demonstrated smooth muscle relaxant activity.

In this double-blind study, twenty patients having G.I. series and exhibiting spasm were randomly selected to receive either 2 cc. of Bentyl or sodium chloride intramuscularly. Ten minutes after the injection another radiograph was taken . . .

. . . Bentyl produced definite relaxation in 8 of 10 patients. The sodium chloride produced relaxation in only 3 of 10. No side effects occurred in either group of patients.



Pylorospasm has almost totally blocked passage of barium meal.



Barium meal beginning to pass 10 minutes after intramuscular injection of 20 mg. Bentyl.

"The correlation of spasm relief and drug given was excellent."

*This drug has been classified "probably" effective in treating functional bowel/irritable bowel syndrome.

†See Warnings, Precautions and Adverse Reactions.

See following page for prescribing information.

Reference:

King, J.C. and Starkman, N.M.: Evaluation of an antispasmodic. Double-blind evaluation to control gastrointestinal spasms occurring during radiographic examination. A preliminary report. Western Med. 5:356-358, 1964.

Merrell

Bentyl[®]

(dicyclomine hydrochloride USP)

Capsules, Tablets, Syrup, Injection

AVAILABLE ONLY ON PRESCRIPTION

Brief Summary

INDICATIONS

Based on a review of this drug by the National Academy of Sciences-National Research Council and/or other information, FDA has classified the following indications as "probably" effective:

For the treatment of functional bowel/irritable bowel syndrome (irritable colon, spastic colon, mucous colitis) and acute enterocolitis.

THESE FUNCTIONAL DISORDERS ARE OFTEN RELIEVED BY VARYING COMBINATIONS OF SEDATIVE, REASSURANCE, PHYSICIAN INTEREST, AMELIORATION OF ENVIRONMENTAL FACTORS.

For use in the treatment of infant colic (syrup).

Final classification of the less-than-effective indications requires further investigation.

CONTRAINDICATIONS: Obstructive uropathy (for example, bladder neck obstruction due to prostatic hypertrophy); obstructive disease of the gastrointestinal tract (as in achalasia, pyloroduodenal stenosis); paralytic ileus, intestinal atony of the elderly or debilitated patient; unstable cardiovascular status in acute hemorrhage, severe ulcerative colitis; toxic megacolon complicating ulcerative colitis; myasthenia gravis. **WARNINGS:** In the presence of a high environmental temperature, heat prostration can occur with drug use (fever and heat stroke due to decreased sweating). Diarrhea may be an early symptom of incomplete intestinal obstruction, especially in patients with ileostomy or colostomy. In this instance treatment with this drug would be inappropriate and possibly harmful. Bentyl may produce drowsiness or blurred vision. In this event, the patient should be warned not to engage in activities requiring mental alertness such as operating a motor vehicle or other machinery or perform hazardous work while taking this drug. **PRECAUTIONS:** Although studies have failed to demonstrate adverse effects of dicyclomine hydrochloride in glaucoma or in patients with prostatic hypertrophy, it should be prescribed with caution in patients known to have or suspected of having glaucoma or prostatic hypertrophy. Use with caution in patients with: Autonomic neuropathy. Hepatic or renal disease. Ulcerative colitis. Large doses may suppress intestinal motility to the point of producing a paralytic ileus and the use of this drug may precipitate or aggravate the serious complication of toxic megacolon. Hyperthyroidism, coronary heart disease, congestive heart failure, cardiac arrhythmias, and hypertension. Hiatal hernia associated with reflux esophagitis since anticholinergic drugs may aggravate this condition.

Do not rely on the use of the drug in the presence of complication of biliary tract disease. Investigate any tachycardia before giving anticholinergic (atropine-like) drugs since they may increase the heart rate. With overdosage, a curare-like action may occur. **ADVERSE REACTIONS:** Anticholinergics/antispasmodics produce certain effects which may be physiologic or toxic depending upon the individual patient's response. The physician must delineate these. Adverse reactions may include: xerostomia; urinary hesitancy and retention; blurred vision and tachycardia; palpitations; mydriasis; cycloplegia; increased ocular tension; loss of taste; headache; nervousness; drowsiness; weakness; dizziness; insomnia; nausea; vomiting; impotence; suppression of lactation; constipation; bloated feeling; severe allergic reaction or drug idiosyncrasies including anaphylaxis; urticaria and other dermal manifestations; some degree of mental confusion and/or excitement, especially in elderly persons; and decreased sweating. With the injectable form there may be a temporary sensation of lightheadedness and occasionally local irritation. **DOSEAGE AND ADMINISTRATION:** Dosage must be adjusted to individual patient's needs.

Usual Dosage: Bentyl 10 mg capsule and syrup: *Adults:* 1 or 2 capsules or teaspoonfuls syrup three or four times daily. *Children:* 1 capsule or teaspoonful syrup three or four times daily. *Infants:* ½ teaspoonful syrup three or four times daily. (May be diluted with equal volume of water.) Bentyl 20 mg: *Adults:* 1 tablet three or four times daily. Bentyl Injection: *Adults:* 2 ml. (20 mg.) every four to six hours intramuscularly only. **NOT FOR INTRAVENOUS USE. MANAGEMENT OF OVERDOSE:** The signs and symptoms of overdose are headache, nausea, vomiting, blurred vision, dilated pupils, hot, dry skin, dizziness, dryness of the mouth, difficulty in swallowing, CNS stimulation. Treatment should consist of gastric lavage, emetics, and activated charcoal. Barbiturates may be used either orally or intramuscularly for sedation but they should not be used if Bentyl with Phenobarbital has been ingested. If indicated, parenteral cholinergic agents such as Urecholine[®] (bethanechol chloride USP) should be used.

Product Information as of October, 1978.

Injectable dosage forms manufactured by CONNAUGHT LABORATORIES, INC., Swiftwater, Pennsylvania 18370 or TAYLOR PHARMACAL COMPANY, Ocatator, Illinois 62525 for MERRELL-NATIONAL LABORATORIES, Division of Richardson-Merrell Inc., Cincinnati, Ohio 45215, U.S.A.

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Cincinnati, Ohio 45215, U.S.A.

CARTAS AL EDITOR

11 de febrero de 1980

Juan Aranda, MD
Editor, Boletín de la
Asociación Médica de Puerto Rico
P. O. Box 9387
Santurce, P. R. 00908

Estimado Dr. Aranda:

Acabo de leer con gran satisfacción la carta del Dr. José H. Amadeo que aparece en la edición del Boletín correspondiente a noviembre de 1979.

Me solidarizo totalmente con su declaración cuando comenta la obvia falta de ética profesional que recientemente se manifestó en un artículo sobre una operación para corregir la obesidad. Una cosa es difundir una información sobriamente y sin ribetes de laudo personal, y otra cosa es permitir que la prensa utilice al médico para artículos sensacionalistas que si bien sirven para vender periódicos sirven también para anunciar al médico de una manera desmedida violando así nuestras más fundamentales normas de ética.

El caso al cual se refiere el Dr. Amadeo no ha sido el único. No hace mucho se publicó otro sobre un dedo amputado que lo iban a unir. Menos mal que ese anuncio parece haberse quedado en un "preliminary report".

Comprendo que la clase médica está siendo sometida a presiones intensas para hacer que sus miembros se anuncien sin limitaciones. No hay nada que le gustaría más a nuestros envidiosos críticos que ver nuestro Código de Ética abolido. Sin embargo, si

nosotros queremos mantener el prestigio y el respeto de los cuales nuestra profesión goza, debemos continuar conduciéndonos de acuerdo a ese código que ha sido y debe seguir siendo nuestra Estrella Polar.

Sinceramente,

José M. Torres Gómez, MD, FACP

CONSEJOS SOBRE LA PRESENTACION DE CASOS

La presentación de un caso en forma clara y concisa es parte fundamental de el adiestramiento de un médico. La presentación debe estar en armonía con el propósito de la misma y los propósitos son numerosos: presentación al facultativo supervisor cuando se pasa visita; presentación a los pares en la entrega de guardia; presentación de las admisiones del día previo en la reunión de la mañana con la facultad, compañeros residentes y estudiantes; presentación a un consultor para obtener su opinión; presentación en conferencias clínico-patológicas o similares. En cada una de las presentaciones ha de regir un contenido variable en los detalles y la profundidad, pero habrán ciertos aspectos comunes.

Los siguientes aspectos son comunes a cualquier presentación: se deberá preservar la confidencialidad de el enfermo y su familia;

se habrá de emplear una terminología científica y correcta en el idioma que se utilice para hacer la presentación; se ofrecerán datos básicos tales como la edad, sexo del paciente, quién informa y confiabilidad. Se seguirá un orden que comenzará con la queja principal, continuará con los datos pertinentes de la enfermedad; los antecedentes que tienen que ver con la misma; los datos familiares y psicosociales de importancia y aquellos de naturaleza ecológica que puedan ser pertinentes.

La exploración física se describirá comenzando por una breve descripción general del paciente seguida de los signos vitales y de la descripción de los hallazgos físicos anormales. Para el peso y la estatura se ofrecerán las porcentilas en que se ubica el paciente. La descripción de anomalías se hará empleando términos científicos y, cuando sea pertinente, medición de las lesiones encontradas.

Seguidamente se presentarán los hallazgos de laboratorio y radiográficos ofreciendo para aquéllos las unidades, los miligramos, los miliequivalentes, etc., según sea el caso.

Después de la presentación de los datos básicos, se ofrecerá el diagnóstico tentativo y la lista de problemas acompañados del plan de acción expresado en términos de procedimientos de diagnóstico, terapéuticos y educativos para el paciente y sus familiares.

Se espera que en las presentaciones que se hacen al pasar visita o en la presentación de casos por la mañana la persona responsable esté preparada para hacerlo de memoria salvo en situaciones de gran complejidad donde no se objeta a que utilice algunas notas sobre datos de laboratorio y otros.

Algunas de las fallas que se ven con frecuencia y deslucen la presentación de un caso son las siguientes:

1. Tratar de hacer la presentación en forma improvisada sin la debida preparación, buscando sobre la marcha los datos pertinentes en el expediente del enfermo.
2. Hacer la presentación con voz apagada e imprecisa.
3. Mezclar idiomas utilizando vocablos para los cuales hay traducciones adecuadas.
4. Ofrecer exceso de información que no viene al caso y omitir aquella que es en realidad pertinente.

José E. Sifontes, MD
Febrero 1980

MOTOR NERVE CONDUCTION INDICATORS IN UREMIC NEUROPATHY

Mitz, M. Prakash A. S., Melvin J., Piering, W.: *Arch. Phys. Med. Rehab.* 61: 45-48, 1980.

Desde el advenimiento del procedimiento de hemodiálisis en la década de los sesenta se ha usado cada vez con mayor importancia la medida de la velocidad de conducción nerviosa en los pacientes con enfermedad renal en etapa terminal como un indicador de cuan adecuada es la terapia recibida. Los nervios más estudiados hasta el momento son el peroneo y ulnar. En este estudio se pretende demostrar que la latencia del nervio facial es un indicador más sensitivo en la neuropatía urémica que los otros usados hasta ahora. En el mismo se incluyeron 84 pacientes con enfermedad renal en etapa terminal y 79 voluntarios normales como control. Al comparar los valores obtenidos se encuentra que en mayor número de pacientes se obtienen valores alterados de velocidad de conducción para el nervio facial que para los demás nervios estudiados: peroneo, mediano, ulnar. Se usó la técnica de Miller y asociados; descrita en el trabajo. Los autores recomiendan el uso del nervio facial en lugar de los corrientemente en uso para el seguimiento de los pacientes renales. Tablas y gráficas incluidas.

(Sometido por Frank W. López, MD)

PSYCHOSEXUAL SEQUELAE TO MASTECTOMY: IMPLICATIONS FOR THERAPEUTIC AND REHABILITATION INTERVENTION

Harold J. May, MD; *J. of Rehab.* 46: 1, 1980.

En el artículo el autor recopila estudios hechos a pacientes que se le ha hecho una mastectomía y como

ésta afecta sus vidas. Se encuentra que la mastectomía conlleva un asalto físico, emocional y sexual a la mujer que la deja vulnerable y en un estado de ambivalencia psicológica. Aunque un crecimiento maligno se ha removido de su cuerpo, la mujer puede tener una percepción de que ha sido mutilada y que no es atractiva sexualmente; por lo tanto, salvarle la vida por medio de una intervención quirúrgica y luego negarle el apoyo emocional necesario para formar un nuevo estilo de vida y aceptar su imagen propia alterada es contradictorio. Además las pacientes con mastectomía parecen recibir gran beneficio de la consejería y rehabilitación psicosexual que se debe implementar desde antes de la cirugía y en el período post-operatorio; pues la intervención temprana ayuda a reducir el trauma psicológico que produce la pérdida de un seno.

Las implicaciones para la educación del consejero y el especialista en rehabilitación son claras. Primero: Estos profesionales de la salud deben sentirse confortables con su propia sexualidad, una persona con dificultad para bregar con su propia sexualidad debe resolver estos problemas antes de intentar consejería o rehabilitación psicosexual, especialmente de una mujer con una mastectomía.

Segundo: El profesional debe tener un conocimiento sólido de la base de la disfunción sexual que pueda provocar la mastectomía y debe ser capaz de utilizar este conocimiento de forma delicada y afectuosa con el paciente.

Si se siguen estos principios un programa responsable de rehabilitación personal y sexual para las pacientes con mastectomía puede implementarse.

(Sometido por Verónica Rodríguez, MD)

PROGNOSTIC VALUE OF A SINGLE EXERCISE TEST 3 WEEKS AFTER UNCOMPLICATED MYOCARDIAL INFARCTION

Davidson DM, De Busk RF - *Circulation* 61: 236, 1980

En este estudio se evalúa el valor predictivo de una prueba de ejercicio en pacientes a las 3 semanas de sufrir un infarto agudo sin complicaciones. Se estudiaron 195 pacientes de los cuales 92 fueron seguidos por 2 años.

En los primeros 82 pacientes se limitó la prueba a una frecuencia cardíaca de 130/min en ausencia de síntomas. Los próximos pacientes no se usó un límite de frecuencia cardíaca. Por análisis estadístico múltiple se encontró que una prueba de ejercicio limitada a menos de 4 mets o con depresión del segmento ST de 2 o más mm predecía una mayor incidencia de infarto recurrente, muerte súbita o paro cardíaco. Angina al ejercicio o depresión del segmento ST de 2 o más mm correlación con cirugía de puentes coronarios. No hubo complicaciones causadas por la prueba.

Concluyen los autores que en pacientes con infartos sin complicaciones una prueba de ejercicio a las 3 semanas no conlleva riesgos mayores y aporta información de gran valor predictivo independientemente de las características clínicas de los pacientes.

(Sometido por Guillermo Cintrón, MD)

EL CULTIVO DE LAVADOS BRONQUIALES EN EL DIAGNOSTICO DE TUBERCULOSIS

P. A. Kvale, MD - *Test No. 76 - 14- 142 agosto 1979.*

“El cultivo de lavados bronquiales es de un valor dudoso en el diagnóstico de Tuberculosis”. Los autores llegaron a esta conclusión luego de un análisis del uso de los lavados bronquiales obtenidos de mil

doce bronchoscopias desde el 1969 hasta 1974 en el Hospital Henry Ford de Detroit. De 859 cultivos de lavados bronquiales 18 o 2.1 por ciento fue positivo para microbacteria tuberculosa. Ninguno fue positivo para micobacteria atípica. En 57 de los 859 casos los cultivos de esputo, lavado gástrico, tejido pulmonar, líquido pleural o materil de biopsia pleural fueron positivos para microbacteria tuberculosa. De esos 57 casos 37 tenían cultivos de lavado bronquiales negativos lo cual significa un 68 por ciento de falsos negativo. De los 18 casos en que los lavados bronquiales fueron positivos en 10 casos se obtuvo el bacilo de otra fuente como esputo, líquido pleural y tejido pulmonar. De los 8 ccasos de los cuales el lavado bronquial fue la única fuente de un cultivo positivo, los resultados fueron falsos en 5. A los 2 años ninguno de los 5 casos desarrolló la enfermedad. En resumen, el lavado bronquial fue la fuente de solamente 3 cultivos positivos verdaderos. Los autores opinan que el uso de anestésico locales y tratamiento de tuberculosis previo son las causas para el gran número de flasos negativos.

(Sometido por Ramón E. Figueroa Lebrón, MD, FCCP, (VA)

POSITIONAL FEED BACK AND ELECTRICAL STIMULATION, AUTOMATED TREATMENT FOR HEMIPLEGIC WRIST

Bowman, BR, Baker LL, Waters, RL: *Arch. Phys. Med. Rehabil.* 60: 497-502, 1980.

La retroalimentación posicional y estimulación eléctrica fueron combinadas como una nueva modalidad de tratamiento para facilitar la extensión de la muñeca en pacientes con accidentes cerebrovasculares. Treinta adultos hemiparéticos que no tenían extensión voluntaria de la muñeca fueron utilizados. A los pacientes del grupo de control se les administró

terapia ocupacional, mientras que al otro grupo se le administró la nueva modalidad. Al final de unas semanas el grupo de estudio demostró 28 por ciento de aumento en torque isométrico de extensión con la muñeca, 30° de extensión y 70 por ciento con 30° de flexibilidad. Los pacientes del grupo de control no demostraron cambios significativos en torque. La nueva modalidad permite control repetitivo de ejercicio isotónico y facilitación de la extensión de la muñeca sin necesidad de tener relación el de supervisión paciente-terapista.

(Sometido por Jesús Maldonado, MD)

HISTOPLASMA MENINGITIS: DIAGNOSTIC VALUE OF CEREBROSPINAL FLUID SEROLOGY

Ann. Intern Med 1980; 92: 189-191.

A pacientes con meningitis crónica y cultivo de líquido cefalorraquídeo negativo se les diagnosticó meningitis por *Histoplasma capsulatum*, basándose en estudios seriados de serología; estos pacientes tenían anticuerpos detectables en el líquido espinal al igual que en el suero. Se le trató a los pacientes exitosamente con anfotericina B y tuvieron respuesta clínica favorable. Los pacientes usados como control que tenían histoplasmosis activa y prueba positiva en suero, pero sin involucramiento meníngeo, no tuvieron anticuerpos en el líquido cefalorraquídeo. A los pacientes con meningitis crónica de causa desconocida se le debe hacer estudios serológicos de suero y líquido espinal de anticuerpos para *H. capsulatum*.

(Sometido por Ramón H. Bermúdez, MD)

THE VALUE OF ORTHOSES FOR PATIENTS WITH DUCHENNE MUSCULAR DYSTROPHY

Fred A. Ziter, MD., Kent G. Allsop Ph D., Physical Therapy, Vol. 59, No. 11, November, 1979.

El uso de ortosis rodilla, tobillo, pie, para prolongar la ambulación en personas con distrofia muscular tipo Duchenne es controversial. Aquellos que promueven su uso, recalcan los beneficios físicos, sociales y psicológicos de caminar con abrazaderas comparado con lo incapacitante que es una silla de ruedas. Los que no favorecen su uso, argumentan que existen frustraciones, inconvenientes y altos costos con el uso de estas abrazaderas que sobrepasan los beneficios que pueden ofrecer en un tipo de enfermedad total como ésta.

Los autores de este trabajo reportan los resultados obtenidos en un estudio de 17 pacientes con distrofia muscular de Duchenne utilizando ortosis de rodilla, tobillo y pie para prolongar la ambulación independiente. Se establecen criterios de efectividad basados en la habilidad de caminar luego de un período de tres meses de ajuste a la ortosis.

Ambuladores efectivos eran considerados aquellos que podían caminar veinte pies en un minuto. Siete pacientes (44 por ciento) reunían los criterios de esta categoría y se beneficiaron grandemente del uso de estos aparatos.

Ambuladores de término medio se consideraron aquellos que podían ambular independiente pero más lentamente, también distancias más cortas, más rápido pero asistidos. En esta categoría fueron clasificados cuatro pacientes (23 por ciento).

Fracasos fueron considerados aquellos que no pudieron alcanzar una ambulación independiente a pesar que ellos podían pararse por períodos cortos. Seis pacientes (35 por ciento) fueron considerados en esta categoría.

Los autores concluyen que el uso de estas ortosis puede ser efectiva en muchos, pero no todos los pacientes con distrofia muscular de Duchenne. Establecen ciertos criterios, como el que el niño haya man-

tenido ambulación independiente por lo menos hasta los diez años y que tenga una fuerza residual de por lo menos 50 por ciento. Que no existan factores que compliquen la situación como obesidad, retardación mental, uso prolongado de sillas de ruedas previo o algún factor psicológico.

(Sometido por Tomás U. Poventud, MD)

SERIAL NERVE CONDITION STUDIES IN CARPAL TUNNEL SYNDROME SECONDARY TO RHEUMATOID ARTHRITIS: PRELIMINARY STUDIES

Nanda Kumar Vemireddi, MD, John B. Redford, MD, Chaiyakiati Na Pombejara, MD., Arch Phys Med. Rehab. 60: 393-396, October, 1979

Veinte pacientes con Artritis Reumatoidea los cuales llevaban los criterios de la Asociación Americana de Reumatismo, fueron examinados clínicamente y con métodos electrodiagnósticos para el Síndrome del Tunel Carpal. De todos, ocho mujeres fueron encontradas con evidencia del Síndrome de Tunel Carpal. Todos fueron seguidos seriadamente con estudios de laboratorios, electrodiagnósticos y clínicamente a intervalos de cuatro meses por un año. Todos los pacientes fueron vistos por un reumatólogo y fueron puestos en terapia anti-inflamatoria, medicamento efectiva. En cada visita se obtuvieron niveles sanguíneos de las drogas utilizadas y pruebas seguidas de la velocidad de sedimentación de los eritrocitos (ESR). Dos de las ocho muñecas fueron inmovilizadas con férulas. Los medicamentos utilizados fueron aspirinas en tres de los pacientes y terapia con oro en otro. Las ocho muñecas estudiadas demostraron una disminución en las prolongadas latencias sensoriales anormales del nervio mediano. Estos hallazgos fueron a la par con una mejoría clínica en las parestesias, disminución en la hinchazón de las articulaciones, ausencia del Signo de Tinel en el nervio mediano y una disminución de la velocidad de sedimentación de los

eritrocitos.

Este estudio nos da una fuerte evidencia que los estudios electrodiagnósticos seriados deben ser usados como un parámetro en el seguimiento de los pacientes con artritis reumatoidea que presentan el Síndrome del Tunel Carpal como consecuencia. También este estudio nos indica que una buena terapia anti-inflamatoria e inmovilización pueden controlar el Síndrome del Tunel Carpal en artritis reumatoidea. Ninguna de las muñecas envueltas en el estudio requirieron de cirugía.

(Seomtido por Tomás U. Poventud, MD)

MOTOR NERVE CONDUCTION INDICATORS IN UREMIC NEUROPATHY

Mitz M, Prakash, AS, Melvin J., Arch Phy Med. Rehab, 61: 1-45-48, January 1980

Ochenta y cuatro pacientes con estadio final de enfermedad renal primaria de duración y severidad variable fueron investigados con una determinación única de la latencia del nervio facial y determinación de la velocidad de conducción nerviosa motora de los nervios peroneo, mediano y ulnar. Evidencia electrofisiológica de neuropatía motora se encontró en 72 pacientes. En el nervio facial, la conducción fue anormal en 68 por ciento; en el nervio mediano fue anormal en 36 por ciento; y en el nervio ulnar fue anormal en 22 por ciento. El nervio facial fue el indicador más sensitivo de neuropatía urémica de los cuatro nervios motores estudiados. Información obtenida "monitoreando" el nervio facial en pacientes con fallo renal crónico añadirá significativamente a la data usada para identificar neuropatía urémica.

Estudios combinados de los nervios facial, mediano y peroneo, deberán identificar la mayor parte de pacientes con neuropatía urémica.

(Sometido por Rafael Alvarez, MD)

Health and Safety Tip

From the American Medical Association

535 North Dearborn Street/Chicago, Illinois 60610

Psychoactive Drugs Alter Mental State

Drugs Alter Mind

Psychoactive drugs are those substances that have the capacity to influence behavior by altering feeling, mood, perception or other mental states.

There are many of these drugs. Some are legal, others are not. Even tobacco and coffee have some psychoactive properties.

The American Medical Association divides psychoactive drugs into four groups — (1) Narcotics, such as heroin, morphine and methadone. (2) Depressants, such as barbiturates, tranquilizers and alcohol. (3) Stimulants, such as amphetamines, cocaine and tobacco, and (4) Hallucinogens, such as LSD, marijuana and peyote.

Dependence on alcohol is by far the most prevalent of all the drug dependencies.

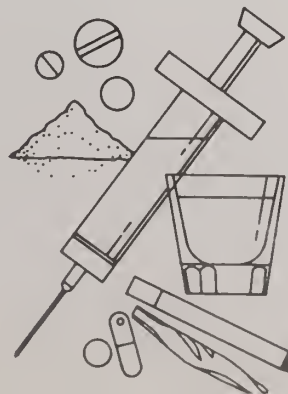
Narcotics originally meant opium and pain relieving drugs related to opium, such as heroin, morphine and codeine. These are made from the opium poppy. Today there also are some synthetics, such as methadone. Heroin is not used medically in this nation. Other opiates are used to

relieve pain, suppress cough and alleviate diarrhea.

Depressants are used to induce sleep and to ease tension. They are used properly in the treatment of certain sleep disorders and anxiety states. They also are subject to abuse. The barbiturates bring sedation and sleep. An overdose can cause coma and heart and respiratory depression. A common mode of suicide is an overdose of barbiturates. Long-term use can bring strong physical dependence.

Stimulants increase activity by stimulating the central nervous system. They include amphetamines, cocaine, Ritalin and Preludin. The amphetamine user has, for a short time, increased mental alertness and sense of well-being. Psychological dependence can develop in a fairly short time. Tolerance develops rapidly and increased amounts of the drug are needed.

Hallucinogens produce illusions. They have no accepted use in medicine. Most potent is LSD. It is legal for use only in government-controlled research projects. Marijuana is in wide use illegally. It brings relaxation. Even small doses may adversely affect driving performance. Many marijuana users tend to experiment with other drugs. Chronic users may become psychologically dependent.



March, 1980
Frank Chappell
Science News Editor
AMA

Tenuate® 

(diethylpropion hydrochloride NF)

Tenuate Dospan®

(diethylpropion hydrochloride NF) controlled-release

AVAILABLE ONLY ON PRESCRIPTION

Brief Summary

INDICATION: Tenuate and Tenuate Dospan are indicated in the management of exogenous obesity as a short-term adjunct (a few weeks) in a regimen of weight reduction based on caloric restriction. The limited usefulness of agents of this class should be measured against possible risk factors inherent in their use such as those described below.

CONTRAINDICATIONS: Advanced arteriosclerosis, hyperthyroidism, known hypersensitivity, or idiosyncrasy to the sympathomimetic amines, glaucoma. Agitated states. Patients with a history of drug abuse. During or within 14 days following the administration of monoamine oxidase inhibitors, (hypertensive crises may result).

WARNINGS: If tolerance develops, the recommended dose should not be exceeded in an attempt to increase the effect; rather, the drug should be discontinued. Tenuate may impair the ability of the patient to engage in potentially hazardous activities such as operating machinery or driving a motor vehicle; the patient should therefore be cautioned accordingly. **Drug Dependence:** Tenuate has some chemical and pharmacologic similarities to the amphetamines and other related stimulant drugs that have been extensively abused. There have been reports of subjects becoming psychologically dependent on diethylpropion. The possibility of abuse should be kept in mind when evaluating the desirability of including a drug as part of a weight reduction program. Abuse of amphetamines and related drugs may be associated with varying degrees of psychologic dependence and social dysfunction which, in the case of certain drugs, may be severe. There are reports of patients who have increased the dosage to many times that recommended. Abrupt cessation following prolonged high dosage administration results in extreme fatigue and mental depression; changes are also noted on the sleep EEG. Manifestations of chronic intoxication with anorectic drugs include severe dermatoses, marked insomnia, irritability, hyperactivity, and personality changes. The most severe manifestation of chronic intoxications is psychosis, often clinically indistinguishable from schizophrenia. **Use in Pregnancy:** Although rat and human reproductive studies have not indicated adverse effects, the use of Tenuate by women who are pregnant or may become pregnant requires that the potential benefits be weighed against the potential risks. **Use in Children:** Tenuate is not recommended for use in children under 12 years of age.

PRECAUTIONS: Caution is to be exercised in prescribing Tenuate for patients with hypertension or with symptomatic cardiovascular disease, including arrhythmias. Tenuate should not be administered to patients with severe hypertension. Insulin requirements in diabetes mellitus may be altered in association with the use of Tenuate and the concomitant dietary regimen. Tenuate may decrease the hypotensive effect of guanethidine. The least amount feasible should be prescribed or dispensed at one time in order to minimize the possibility of overdosage. Reports suggest that Tenuate may increase convulsions in some epileptics. Therefore, epileptics receiving Tenuate should be carefully monitored. Titration of dose or discontinuance of Tenuate may be necessary.

ADVERSE REACTIONS: *Cardiovascular:* Palpitation, tachycardia, elevation of blood pressure, precordial pain, arrhythmia. One published report described T-wave changes in the ECG of a healthy young male after ingestion of diethylpropion hydrochloride. *Central Nervous System:* Overstimulation, nervousness, restlessness, dizziness, jitteriness, insomnia, anxiety, euphoria, depression, dysphoria, tremor, dyskinesia, mydriasis, drowsiness, malaise, headache; rarely psychotic episodes at recommended doses. In a few epileptics an increase in convulsive episodes has been reported. *Gastrointestinal:* Dryness of the mouth, unpleasant taste, nausea, vomiting, abdominal discomfort, diarrhea, constipation, other gastrointestinal disturbances. *Allergic:* Urticaria, rash, ecchymosis, erythema. *Endocrine:* Impotence, changes in libido, gynecomastia, menstrual upset. *Hematopoietic System:* Bone marrow depression, agranulocytosis, leukopenia. *Miscellaneous:* A variety of miscellaneous adverse reactions has been reported by physicians. These include complaints such as dyspnea, hair loss, muscle pain, dysuria, increased sweating, and polyuria.

DOSAGE AND ADMINISTRATION: Tenuate (diethylpropion hydrochloride): One 25 mg. tablet three times daily, one hour before meals, and in mid-evening if desired to overcome night hunger. Tenuate Dospan (diethylpropion hydrochloride) controlled-release: One 75 mg. tablet daily, swallowed whole, in mid-morning. Tenuate is not recommended for use in children under 12 years of age.

OVERDOSAGE: Manifestations of acute overdosage include restlessness, tremor, hyperreflexia, rapid respiration, confusion, assaultiveness, hallucinations, panic states. Fatigue and depression usually follow the central stimulation. Cardiovascular effects include arrhythmias, hypertension or hypotension and circulatory collapse. Gastrointestinal symptoms include nausea, vomiting, diarrhea, and abdominal cramps. Overdose of pharmacologically similar compounds has resulted in fatal poisoning, usually terminating in convulsions and coma. Management of acute Tenuate intoxication is largely symptomatic and includes lavage and sedation with a barbiturate. Experience with hemodialysis or peritoneal dialysis is inadequate to permit recommendation in this regard. Intravenous phenolamine (Regitine®) has been suggested on pharmacologic grounds for possible acute, severe hypertension, if this complicates Tenuate overdosage.

Product Information as of April, 1976

MERRELL-NATIONAL LABORATORIES Inc.

Cayey, Puerto Rico 00633

Direct Medical Inquiries to

MERRELL-NATIONAL LABORATORIES

Division of Richardson-Merrell Inc.

Cincinnati, Ohio 45215, U.S.A.

Licensors of Merrell®

References: 1. Citations available on request from Medical Research Department, MERRELL-NATIONAL LABORATORIES, Cincinnati, Ohio 45215. 2. Hoekenga, M.T., O Gillon [Dillon], R.H., and Leyland, H.M.: A comprehensive review of diethylpropion hydrochloride. In, Central Mechanisms of Anorectic Drugs, S. Garattini and R. Samanin, Ed., New York, Raven Press, 1978, pp. 391-404.

Merrell

**Overweight may not always be simple...
complications can develop*.
Complicated or not...**

Tenuate[®] Dospan[®] ^{IV} **(diethylpropion hydrochloride NF)** **75 mg. controlled-release tablets**

A useful short-term adjunct in an indicated weight loss program.

Overweight patients in certain diagnostic categories often require strict appetite control and a successful program of weight reduction may tend to diminish the incidence or severity of the complications in some patients. Diethylpropion hydrochloride has been reported useful in such patients and while it is not suggested that Tenuate itself in any way reduces the complications of overweight, it may have a useful place as a short-term adjunct in a prescribed dietary regimen. **Tenuate should not be administered to patients with severe hypertension; see additional Warnings and Precautions on the opposite page.**

In uncomplicated overweight.

Many patients, on the other hand, present with excess fat but no disease. While this condition is often termed uncomplicated obesity, complications of both a social and a psychologic nature may be distressingly real for the patients. In these cases, a short-term regimen of Tenuate can help reinforce your dietary counsel during the important early weeks of an indicated weight loss program.

Clinical effectiveness.

The anorectic effectiveness of diethylpropion hydrochloride is well documented. No less than 16 separate double-blind, placebo-controlled studies attest to its usefulness in daily practice.¹ And the unique chemistry of Tenuate provides "...anorectic potency with minimal overt central nervous system or cardiovascular stimulation."² Compared with the amphetamines, diethylpropion has minimal potential for abuse.

**Tenuate—it makes sense.
And it's responsible medicine.**

*Studies have shown that obesity is associated with an increased incidence of hypertension, symptomatic heart disease, adult-onset diabetes, and other diseases.

Merrell

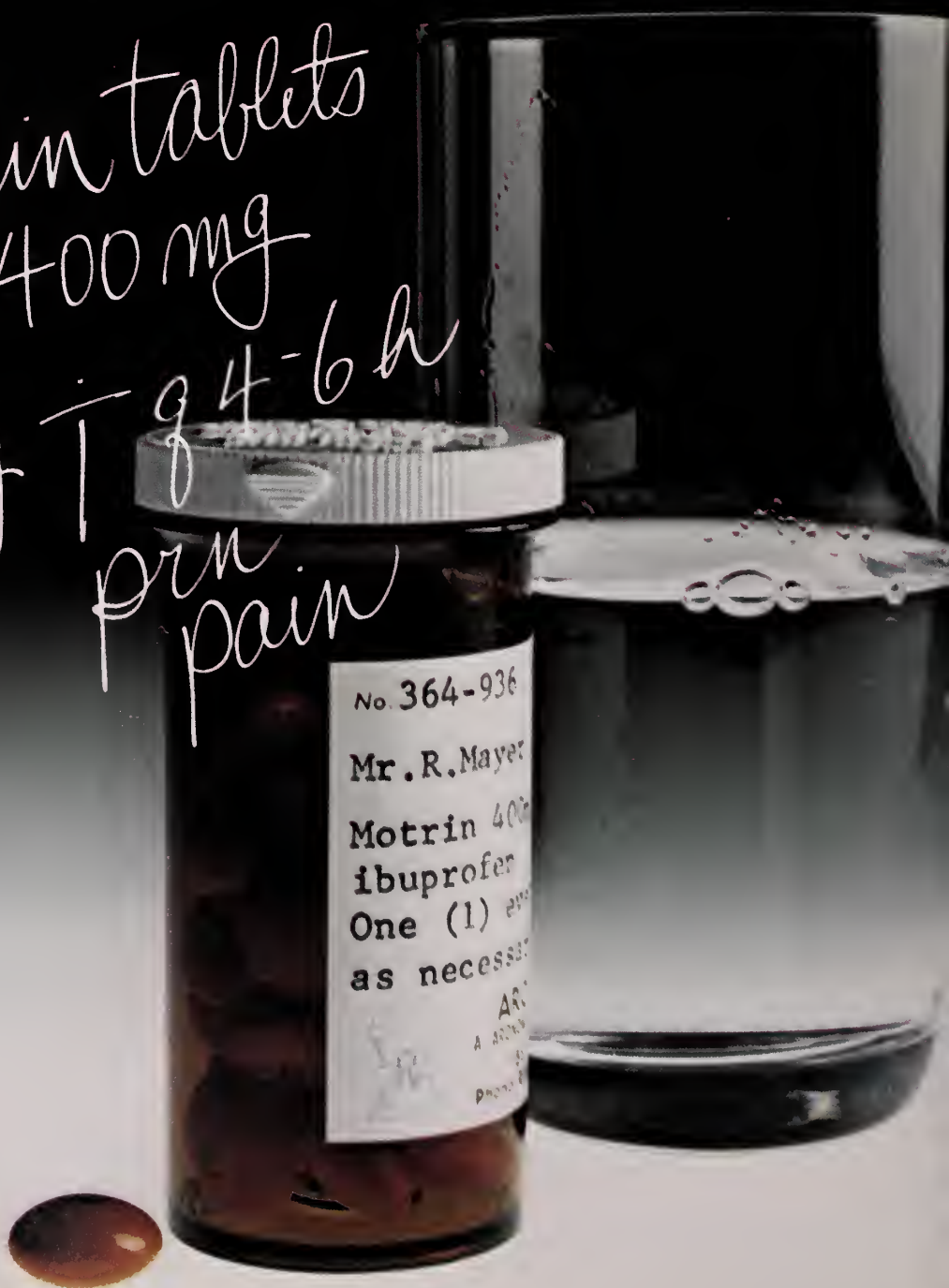


For prescribing information see opposite page

A well-tolerated, nonnarcotic prescription for pain

Motrin tablets
400 mg

Sig T q 4-6 h
prn
pain



Motrin[®] now proved an effective analgesic for mild to moderate pain

Motrin 400 mg provided greater relief of pain than did propoxyphene 65 mg in controlled clinical pain studies.

Time after drug administration (hour)		.5	1	2	3	4
Mean relief-of-pain scores* (No. patients reporting)	Motrin 400 mg ibuprofen	.89 (108)	1.25 (108)	1.36 (108)	1.28 (107)	1.19 (106)
	Darvon 65 mg propoxyphene	.66 (100)	.99 (99)	1.13 (96)	.99 (96)	.80 (96)
Statistical significance		p<0.02	p<0.01	p<0.05	p<0.02	p<0.002

*0 = No relief 1 = Partial relief 2 = Complete relief

Data on file at The Upjohn Company

Motrin demonstrated statistically significant greater relief of pain than did Darvon at all time intervals.

Motrin 400^{TABLETS}mg
ibuprofen, Upjohn

- Not a narcotic • Not addictive • Not habit forming
- Rapid analgesic action • Indicated in acute and chronic pain
- Well tolerated. The most common side effect with Motrin is mild gastrointestinal disturbance.

Please turn the page for a brief summary of prescribing information.

Motrin[®] (ibuprofen) now proved an effective analgesic for mild to moderate pain

Motrin[®] Tablets (ibuprofen, Upjohn)

Indications and Usage: Treatment of signs and symptoms of rheumatoid arthritis and osteoarthritis during acute flares and in long-term management. Safety and efficacy have not been established in Functional Class IV rheumatoid arthritis.

Relief of mild to moderate pain.

Contraindications: Individuals hypersensitive to it, or with the syndrome of nasal polyps, angioedema and bronchospastic reactivity to aspirin or other nonsteroidal anti-inflammatory agents (see WARNINGS).

Warnings: Anaphylactoid reactions have occurred in patients with aspirin hypersensitivity (see CONTRAINDICATIONS).

Peptic ulceration and gastrointestinal bleeding, sometimes severe, have been reported. Ulceration, perforation, and bleeding may end fatally. An association has not been established. Motrin should be given under close supervision to patients with a history of upper gastrointestinal tract disease, only after consulting ADVERSE REACTIONS.

In patients with active peptic ulcer and active rheumatoid arthritis, nonulcerogenic drugs, such as gold, should be tried. If Motrin must be given, the patient should be under close supervision for signs of ulcer perforation or gastrointestinal bleeding.

Precautions: Blurred and/or diminished vision, scotomata, and/or changes in color vision have been reported. If these develop, discontinue Motrin and the patient should have an ophthalmologic examination, including central visual fields.

Fluid retention and edema have been associated with Motrin; use with caution in patients with a history of cardiac decompensation.

Motrin can inhibit platelet aggregation and prolong bleeding time. Use with caution in persons with intrinsic coagulation defects and those on anticoagulant therapy.

Patients should report signs or symptoms of gastrointestinal ulceration or bleeding, blurred vision or other eye symptoms, skin rash, weight gain, or edema.

To avoid exacerbation of disease or adrenal insufficiency, patients on prolonged corticosteroid therapy should have therapy tapered slowly when Motrin is added.

Drug interactions. Aspirin: used concomitantly may decrease Motrin blood levels. Coumarin: Bleeding has been reported in patients taking Motrin and coumarin.

Pregnancy and nursing mothers: Motrin should not be taken during pregnancy or by nursing mothers.

Adverse Reactions

Incidence greater than 1%

Gastrointestinal: The most frequent type of adverse reaction occurring with Motrin is gastrointestinal (4% to 16%). This includes nausea,* epigastric pain,* heartburn,* diarrhea, abdominal distress, nausea and vomiting, indigestion, constipation, abdominal cramps or pain, fullness of the GI tract (bloating and flatulence). **Central Nervous System:** Dizziness,* headache, nervousness. **Dermatologic:** Rash* (including maculopapular type), pruritus. **Special Senses:** Tinnitus. **Metabolic:** Decreased appetite, edema, fluid retention. Fluid retention generally responds promptly to drug discontinuation (see PRECAUTIONS).

*Incidence 3% to 9%.

Incidence less than 1 in 100

Gastrointestinal: Upper GI ulcer with bleeding and/or perforation, hemorrhage, melena. **Central Nervous System:** Depression, insomnia. **Dermatologic:** Vesiculobullous eruptions, urticaria, erythema multiforme. **Cardiovascular:** Congestive heart failure in patients with marginal cardiac function, elevated blood pressure. **Special Senses:** Amblyopia (see PRECAUTIONS). **Hematologic:** Leukopenia, decreased hemoglobin and hematocrit.

Causal relationship unknown

Gastrointestinal: Hepatitis, jaundice, abnormal liver function. **Central Nervous System:** Paresthesias, hallucinations, dream abnormalities. **Dermatologic:** Alopecia, Stevens-Johnson syndrome. **Special Senses:** Conjunctivitis, diplopia, optic neuritis. **Hematologic:** Hemolytic anemia, thrombocytopenia, granulocytopenia, bleeding episodes. **Allergic:** Fever, serum sickness, lupus erythematosus syndrome. **Endocrine:** Gynecomastia, hypoglycemia. **Cardiovascular:** Arrhythmias. **Renal:** Decreased creatinine clearance, polyuria, azotemia.

Overdosage: In cases of acute overdosage, the stomach should be emptied. The drug is acidic and excreted in the urine, so alkaline diuresis may be beneficial.

Dosage and Administration: Rheumatoid and osteoarthritis, including flares of chronic disease: Suggested dosage is 300, 400 or 600 mg t.i.d. or q.i.d.

Mild to moderate pain: 400 mg every 4 to 6 hours as necessary for relief of pain.

Do not exceed 2400 mg per day.

Caution: Federal law prohibits dispensing without prescription.

For additional product information, see your Upjohn representative or consult the package insert.

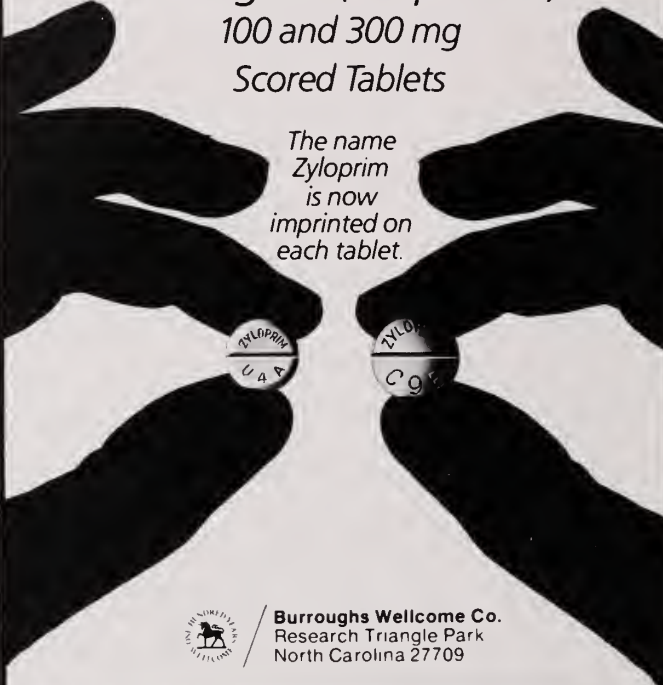
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ZYLOPRIM[®]

the original (allopurinol)

100 and 300 mg
Scored Tablets

The name
Zyloprim
is now
imprinted on
each tablet.



 **Burroughs Wellcome Co.**
Research Triangle Park
North Carolina 27709

ST. PAT'S DAY: GREEN MERRIMENT

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1980

SPRING: A NEW BEGINNING

MED B-4-S

Upjohn

THE UPJOHN COMPANY
Kalamazoo, Michigan 49001 USA

THERAPIES FOR CEREBRAL PALSY

Marguis, P. *Am. Family Physician* 19: 6 - 101-105, June, 1979

Al repasar el racional y los resultados terapéuticos de las diferentes disciplinas envueltas en el tratamiento de parálisis cerebral, este artículo asiste a los médicos de familia que trabajan con varias disciplinas para ayudar a pacientes con esta enfermedad. Importantes consideraciones en los tipos de tratamiento discutidos son:

1. terapia física — un multi-abarcador prospectivo, estudio controlado se dice necesitar para confirmar efectividad,
2. férulas — propósitos de ambas "full control" y "short leg braces" son explicados.
3. terapia ocupacional — ofrece invaluable destrezas de ayuda propia, diseños de equipo adaptativo, e instrucciones para los padres,
4. cirugía ortopédica — aunque procedimientos quirúrgicos tienen un rol importante en el manejo de parálisis cerebral, han sido relativamente inefectivos en el tratamiento de envolvimiento de extremidad superior y son de poco valor para pacientes con enfermedad extrapiramidal,
5. neurocirugía — el cual es un tratamiento experimental al presente,

6. medicamentos — el uso de benceto diazepinas, dantrolene sódico y de levodopa es discutido.

(Sometido por Rafael Alvarez, MD)

ELECTROMYOGRAPHIC FEEDBACK EFFECT ON VOLUNTARY MUSCLES CONTRACTION IN PARALYTIC SUBJECTS

Middaugh, SJ, Miller, MC: *Arch. Phys. Med. Rehabil* 61: 2y - 29, 1980.

Para evaluar la eficacia y función de la retroalimentación electromiográfica en la reeducación muscular se evaluaron las contracciones musculares esqueléticas con y sin este tipo de retroalimentación. Esto se llevó a cabo bajo condiciones experimentales controladas en sujetos humanos con parálisis debido a daño cerebral o con daño al sistema nervioso periférico. Cada sujeto produjo 12 contracciones sostenidas por 30 segundos en músculos cuya suma estaba bajo los niveles funcionales. Se hicieron pruebas con y sin retroalimentación. Para el tiempo de la segunda sesión la contracción muscular voluntaria había mejorado significativamente. Este diferencial se desarrolló durante los primeros 10 segundos de la contracción y se mantenía constante hasta el final de los 30 segundos. La respuesta a la retroalimentación electromiográfica no estaba íntimamente relacionada con el tipo o duración de la lesión ni con la edad del paciente.

(Sometido por Jesús Maldonado, MD)

A Videotape Service **DIAGNOSTIC ULTRASOUND** is being offered for rental or purchase by the Ultrasound Section of the Department of Radiology, the University of California, San Diego. The Faculty are: Barbara B. Gosink, MD, George R. Leopold, MD and William Scheible, MD. The series covers selected topics in Diagnostic Ultrasound, each 40-55 minute tape produced in the studio since June 1979. The programs are available in U-matic 3/4 in. video cassette and Sony Beta-max and VHS 1/2 in. video cassette.

For program brochure and registration information, please contact: Elizabeth Novak, Ultrasound Section, University Hospital, 225 W. Dickinson St., San Diego, California 92103. (714) 294-6657.

Los Departamentos de Medicina y Medicina Familiar de la Facultad de Medicina de la Universidad de Miami, el Centro Médico de la Administración de Veteranos de Miami y la Empresa Farmacéutica CIBA anuncian una Presentación de HORIZONTES MEDICOS ® — **SEMINARIO SOBRE HIPERTENSION Y NEFROLOGIA EN ESPAÑOL** - Viernes y Sábado 16-17 de mayo de 1980 - Konover Hotel, 5445 Collins Avenue, Miami Beach, Florida 33140 - Teléfono (305) 865-1500.

AMERICAN COLLEGE OF CARDIOLOGY invites you to a program directed by: Borys Surawicz, MD, FACC - **ADVANCED CARDIAC ELECTROPHYSIOLOGY FOR CARDIOLOGISTS** - June 2, 3 and 4, 1980, to be offered at the Heart House Learning Center, 9111 Old Georgetown Road, Bethesda, Maryland.

The American College of Cardiology and Cardiovascular Center of the University of Nebraska Medical Center, Omaha, Nebraska announce **(Sixth Annual) TUTORIALS IN THE TETONS: CARDIAC EMERGENCIES, New Diagnostic and Therapeutic Advances** - August 23, 24, and 25, 1980 - To be presented at: Jackson Lake Lodge, Grand Teton National Park, Moran, Wyoming.

NEW ORLEANS INTERNAL MEDICINE BOARD REVIEW COURSE - September 2-7, 1980 - Hyatt Regency Hotel. For information write to: New Orleans Board Review, 1430 Tulane Avenue, New Orleans, Louisiana 70112.

NOTICIAS

AMA NEWS:

CONGRESS ON MEDICAL EDUCATION SET FOR NEXT APRIL IN CHICAGO

CHICAGO — The 76th Congress on Medical Education will be held April 24-26 in Chicago (Palmer House).

Co-sponsors of the Congress are the American Medical Association, the Association for Hospital Medical Education, and the Federation of State Medical Boards of the United States.

Theme of the Congress will be: Dilemmas of the Decade — Medical Education and Licensure.

Dr. Donald Kennedy, vice president and provost, Stanford University, former commissioner of the U. S. Food and Drug Administration, will be the keynote speaker at the opening session. Heading a panel on generalism and specialism during the first morning's program will be Norman Cousins, chairman of the editorial board, *Saturday Review*, and senior lecturer in medical humanities, University of Southern California at Los Angeles School of Medicine.

Newton Minow, senior partner of the law firm of Sidley and Austin, Chicago, and former chairman of the Federal Communications Commission, will deliver the major address of the second day's session, speaking on The Regulation of Medicine.

Theodore Cooper, M.D., dean at Cornell University Medical Center, former Assistant Secretary for Health of the U. S. Department of Health, Education and Welfare, will keynote a session with an address on Factors Affecting Medical Progress.

Groups of distinguished panelists will join the keynote speakers in expanding on various aspects of the convention theme of the dilemmas facing medical education and licensure of physicians.

Appearing with Mr. Cousins will be William D. Holden, MD, chairman of the National Board of Medical Examiners; Herbert A. Holden, MD, past president of the American Academy of Family Physicians,

and John M. Eisenberg, MD, of the University of Pennsylvania School of Medicine.

A panel on Public and Professional Perspectives will include Donald S. Winston, MD, chairman of the former AMA Resident Physician Section's Workshop on Cost Containment; Robert T. Kelly, MD, chairman of the AMA Council on Medical Service; Hugh Tilson, MD, director, Department of Health Services, State of North Carolina, and Henry G. Cramblett, MD, dean, Ohio State University College of Medicine.

On the panel with Mr. Minow will be Thomas B. Ferguson, MD, president, Council of Medical Specialty Societies; E. Harvey Estes, MD, chairman, Department of Community and Family Medicine, Duke University Medical Center; Howard G. McQuarrie, MD, of the Utah Board of Registration; John H. Morton, MD, past president, Federation of State Medical Boards, and John C. Sage, MD, of the Nebraska Board of Medical Licensure.

The panel with Dr. Cooper will include Robert S. Stone, MD, dean of Texas A & M College of Medicine, Geoffrey Segar, an Indianapolis attorney, and Walter T. Winslow, Jr., of the Bureau of Competition of the Federal Trade Commission.

Congress registrants may attend all-day workshops sponsored by the Federation of State Medical Boards of the United States on Wednesday, April 23, and a 50th Anniversary Symposium on Allied Health sponsored by the AMA on Friday and Saturday, April 25 and 26. A workshop on graduate education also will be offered, Friday afternoon, April 25.

Further information on the Congress is available from the office of Dr. John Fauser, Group on Medical Education, American Medical Association, 535 N. Dearborn St., Chicago, Ill 60610.

AMA ISSUES NEW EDITION OF ALLIED HEALTH EDUCATION DIRECTORY

CHICAGO — The Eighth Edition of the American Medical Association's *Allied Health Education Directory* is off the press this winter.

The Directory is the only comprehensive and authoritative source of information available on the 24 allied health careers and the almost 3,000 educational programs accredited by the Committee on Allied Health Education and Accreditation of the AMA.

The Directory serves as a guide for student counselors in advising students on allied health careers. It encompasses facts on career opportunities, job descriptions, educational programs and financial aid. It is an important reference source for librarians, educators, hospital administrators, physicians and others.

The 24 allied health careers include assistant to the primary care physician, emergency medical technician-paramedic, medical assistant, medical laboratory technician, nuclear medicine technology and surgeon's assistant.

There is an alphabetical listing of some 1,700 institutions that sponsor the accredited educational program, plus another listing of each of the 2,951 programs categorized by occupational type and then arranged by city, state, and sponsoring institution.

A separate section includes brief synopsis of the job duties, employment characteristics, educational prerequisites, registration or certification opportunities, and licensure requirements for each of the 24 occupations.

The Directory was prepared by the AMA's Department of Allied Health Education and Accreditation. Director is John E. Beckley, PhD. Copies are available from: Order Department, OP-391; American Medical Association, P. O. Box 821, Monroe, WI 53566. Single copies are \$12.00.

*AMERICAN MEDICAL ASSOCIATION TO HOLD
FOURTH NATIONAL CONFERENCE ON THE IM-
PAIRED PHYSICIAN*

CHICAGO — The Fourth National Conference on the Impaired Physician is scheduled for Oct. 29 - Nov. 1 in Baltimore MD., (Lord Baltimore Hotel).

Sponsored by the American Medical Association Department of Mental Health in cooperation with the Medical and Chirurgical Faculty of Maryland, the conference will focus on all aspects of impairment, including prevention. Special emphasis will be given to medical students, residents, women physicians, senile physicians and the medical marriage.

Conference participants will meet both in plenary sessions and in discussion groups. Topics to be addressed include: case-finding, confrontation, treatment issues, re-entry problems, legal aspects of impairment, hospital and medical society programs, student and resident well-being, curriculum development and auxiliary programs. Evening sessions will include a meeting of the International Doctors in Alcoholics Anonymous; sessions on epidemiology, family dynamics, and coping with practice stress; and support groups for students and residents.

Further information is available from the Department of Mental Health, American Medical Association, 535 N. Dearborn St., Chicago, IL 60610.

OBESITY ESCALATES RISK OF EARLY DEATHS

CHICAGO — Excessive extra weight increases the risk of early death by very high margins, says a report in the Feb. 1 Journal of the American Medical Association.

Dr. Ernest J. Drenick of the Veterans Administration Wadsworth Hospital Medical Center, Los Angeles, reports on a study of 200 obese men who averaged more than 300 pounds each. They had come to the hospital to try to lose weight. Most did not succeed. Followup period was for seven years.

The younger obese men, age 25 to 34, had a 12-fold excess death rate above men of normal weight in the same age bracket, Dr. Drenick says. In the age group 35 to 44, the death rate increased sixfold. The ratio diminished with advancing age. Cardiovascular disease was reported as the most frequent cause of death. Fifty of the 200 men died during the course of the study.

The heavier the man, the greater the risk of early death, he found.

DISTANCE RUNNING STUDIED AS POSSIBLE SAFEGUARD AGAINST CORONARY DISEASE

CHICAGO — Does distance running help protect the runner against the development of coronary disease?

Possibly. But medical science cannot say this positively.

Another research report on the subject is published in the Feb. 8 Journal of the American Medical Association. It involves a study of physical attributes of 50 physician runners, members of the American Medical Joggers Association. They were compared to 50 non-running doctors.

The runners had significantly lower pulse rates and lower relative weights. They also had elevated high-density lipo-protein (HDL) cholesterol levels in their blood. It has been postulated that the HDL affords protection against coronary artery disease by acting as a clearing agent in removing cholesterol from body cells, says Dr. Marvin M. Adner of the Framingham (Mass.) Union Hospital.

If the theory that increased HDL lowers risk of heart disease is correct, then distance runners should have a lower risk of developing coronary artery disease than nonrunners, Dr. Adner says.

"The hypothesis that exercise elevates HDL cholesterol levels, resulting in protection from coronary artery disease, is an attractive, well-publicized theory. Undoubtedly, it is an important motivating

factor for those millions of Americans who have taken up distance running. Although reasonable, this hypothesis remains unproved. It is hoped that the observations made over a period of years on the long-distance runners will clarify the issue."

CORONARY BYPASS SURGERY PERMITS MEN TO STAY AT WORK

CHICAGO — Is the coronary bypass operation to relieve sharp chest pains worthwhile from the economic viewpoint? Do those undergoing the operation go back to work?

There have been conflicting reports on this question in recent years. In the Feb. 8 Journal of the American Medical Association, a Milwaukee research unit reports that the operation does indeed permit men to continue to earn a living, if it is performed in their younger years.

For those men under age 55 at the time of surgery, 90 per cent were employed four years later, says Alfred J. Anderson of the Medical College of Wisconsin, Milwaukee. The percentage drops as age advances. Of those 55 to 59 at time of surgery, 68 per cent were working four years later. Of those 60 and over, 44 per cent were still at work after four years.

Physical requirements of the job were an important factor in decisions to return to work, he says. Also involved were return of the chest pains (angina pectoris) after the operation, a previous heart attack, and age at time of the operation.

Of the patients who had not been working prior to the operation, only 22 per cent were employed four years later.

The study involved 564 male patients who had the operation in two Milwaukee area hospitals over a five-year period.

Mr. Anderson concludes:

"Our results indicate that a large majority of younger patients with aortocoronary bypass operation who were employed before the operation and

have returned to work one year after the operation remained employed for the additional three years. The decision not to remain employed is more prevalent among the older patients."

THE MAIN HEALTH VALUE OF SAUNAS? IT FEELS SO GOOD WHEN YOU QUIT

CHICAGO — Arc steam rooms, saunas and hot tubs of any real physical usefulness?

Probably not. But it feels so good when you quit.

This is the comment of an Illinois doctor, writing in the January 25 Journal of the American Medical Association.

Saunas and steam baths have been used for many centuries by people of all ages because of the feeling of well-being they are said to produce, writes Dr. David I. Abramson of Oak Park, Ill.

However, Dr. Abramson says, it is difficult to demonstrate any beneficial effect on the health or physical capacity of the person who uses them. The body loses considerable salt through perspiration. Those with high blood pressure experience a drop in pressure in the saunas, but the effect is temporary. Persons with hardening of the arteries, heart difficulties and hyperthyroidism most definitely should not use the heat treatments, Dr. Abramson declares.

"Perhaps the sense of well-being that occurs after the person leaves the hot, humid environment could be compared with the great feeling of relief experienced by the patient who has been suffering from severe pain and suddenly finds that he has become free of symptoms."

EXPLODING WHISKEY BARRELS IS NEW SAFETY HAZARD

CHICAGO — A new safety hazard has appeared on the American scene this winter — exploding whiskey barrels.

Writing in the Jan. 25 Journal of the American Medical Association, Dr. David W. Becker, Jr. of Boise, Idaho, tells of children injured when a used whiskey barrel, purchased by the family as a decorative yard ornament, exploded when a child struck a match to explore the barrel's interior.

The explosion was heard at the end of the block, Dr. Becker says. The lid of the barrel was blown over the house into the front yard. A 9-year-old girl was burned on the face, chest and hands. On the same day, two other children were treated in the emergency room of a hospital for minor injuries from another exploding whiskey barrel.

The used barrels are seen with ever-increasing frequency for sale at roadside stands and lumber yards, the Idaho doctor reports. Under proper conditions, the residual fumes contained in whiskey barrels are potentially very explosive, he says.

NEWS OF EMERGENCY MEDICINE — FROM THE AMERICAN COLLEGE OF EMERGENCY PHYSICIANS

Not many participants in softball games think of their sport as being particularly hazardous. But cases reported in the March issue of Annals of Emergency Medicine provide information that should be of concern to athletes, coaches and emergency physicians.

Athletes should "avoid situations likely to result in blunt impact to the central chest", according to Errol D. Green, MD, principal author of "Cardiac Concussion Following Softball Blow to the Chest". The article reports on two cases of sudden death in young men following softball blows to the chest. Dr. Green and his fellow authors are from the Departments of Emergency Medicine and Pathology at Edward W. I

Sparrow hospital in Lansing, Michigan; and the Office of the Medical Examiner of the State of Rhode Island in Providence.

"Sudden death from seemingly trivial blunt trauma to the chest, and with no intrathoracic injury demonstrable at autopsy, is distinctly uncommon," Dr. Green writes, "but such deaths have been reported following a blow to the chest from a stick, a pitched ball, a softball, and a punch during a boxing match." The blow is described as a cardiac concussion.

Similarly, Daniel F. Danzl, MD, principal author of "Ventricular Septal Defect Following Blunt Chest Trauma," cautions emergency physicians that blunt impacts to the chest can result in cardiac injury.

Dr. Danzl, together with Donald M. Thomas, MD, and Jon W. Miller, MD, all of the Department of Emergency Medicine at University Hospital, University of Louisville in Louisville, Kentucky, concludes that blunt chest trauma, such as that caused by a wrestler being "shouldered" in the chest during a match, may cause a lesion in the ventriculum of the heart.

Though the cases reported by these two different studies were accidents which infrequently happen in the ball park or gymnasium, the likelihood of recovery when such an accident does occur is poor.

Detailed accounts of the sports accidents are presented in *Annals of Emergency Medicine*, the monthly clinical journal of the American College of Emergency Physicians and the University Association for Emergency Medicine.

Campers, hikers, and sportsmen beware! The possibility of injury or death from being struck by lightning is not as unlikely as it may seem. Approximately 300 persons are killed by lightning each year in the United States — more than are killed by tornadoes.

Because few physicians have had extensive experience with lightning injuries, and a relatively

small number cases of lightning injury or death are reported, medical studies have been limited. Mary Ann Cooper, MD, associate director of the Emergency Unit at Creighton University in Omaha, Nebraska, recently completed a study of 66 cases of lightning injury and reported the results in the March issue of *Annals of Emergency Medicine*.

Data from the study indicated that 30 percent of the victims seriously injured by lightning died. The injuries sustained included burns to the head, trunk, arm and leg; cardiopulmonary arrest; paralysis; and loss of consciousness. The mortality rate of persons struck by lightning who suffered cardiopulmonary arrest was very high (77 percent).

"Many less severe injuries go unreported and probably occur four or five times more frequently than fatal injuries," Dr. Cooper writes, "thus the overall prognosis for survival is very good."

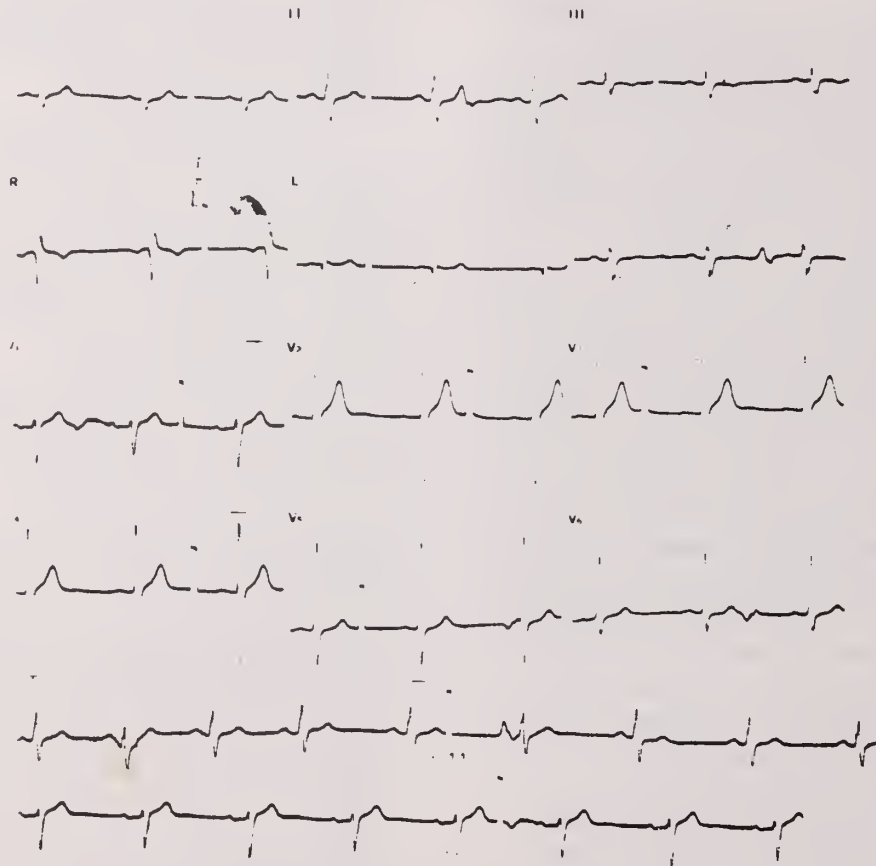
Persons who are in the open or carrying metal objects, such as umbrellas or golf clubs, significantly increase their chances of a direct strike by lightning during the right atmospheric conditions. Even a hair-pin will increase the chances, according to Dr. Cooper.

Lightning injuries are similar to other high voltage electrical injuries in that patients are frequently burned in both kinds of accidents. Lightning may reach energies of a 100 million volts and over 200,000 amperes peak current, levels of energy seldom obtained in high voltage injuries, according to the study. However, lightning is direct current which is less dangerous than the alternating current most frequently associated with other electrical accidents. Lightning, is theorized, flows around the outside of the body of the victim rather than through the victim. Therefore, the victims skin perspiration may be vaporized and his clothes and shoes may blast apart. This "flash-over" phenomenon may result in the victim sustaining less injury than would be expected from equal currents encountered in a high voltage electrical injury.

Annals of Emergency Medicine, the clinical journal of the American College of Emergency Physicians and the University Association for Emergency Medicine, contains Dr. Cooper's complete manuscript, which discusses different types of injuries resulting from a lightning stroke, the physics of lightning, and the difference between a lightning and a high voltage injury.

ELECTROCARDIOGRAM OF THE MONTH

This electrocardiogram (ECG), Figure 1 A, was obtained from an essentially asymptomatic 25-year-old male.



The diagnosis is (choose one or more than one):

1. Normal ECG
2. Normal variant
3. Abnormal ECG
4. If abnormal, the specific diagnosis (es)is (are)

-
5. A. Artifacts
B. If so, what type of artifact?
 6. None of the above.

Answer

Hiccups (singultus)

Borderline left anterior hemiblock (LAH) - block of the superior division of the left bundle branch.

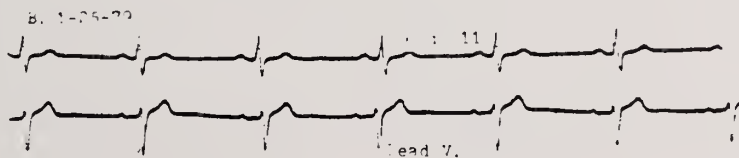
Hiccup is a brief spasm or clonic contraction of the diaphragm (and accessory muscles of respiration), reflecting their electrical activities or action potentials.

Bizarre deflections are visualized in leads 11, aVF (diphasic, mainly upright), V₁, V₅ and V₆ (diphasic, mainly inverted), not related to the QRS complexes and at times distorting the P and T waves. These are called "myogram" artifacts. A different deflection may be seen called "mechanogram" artifact that represents mechanical activity of extracardiac tissues (body vibrations) following each violent contraction of the diaphragm. The myogram has been described in the standard and limb leads and the mechanogram in the precordial leads. The waves may actually be a combination of a myogram and mechanogram. Hiccup artifacts must be differentiated from labored respiration artifacts, atrial dissociation, parasystole and ventricular ectopy.

The QRS axis is - 30 degrees. Tiny q waves are evident in V₂₋₃; taking these leads one inter-space lower may clarify their significance. An incomplete right bundle branch block could be suspected also (moderately wide S waves in leads 1, V₅₋₆ and R in aVR), although S waves are components of a LAH alone.

Six days later (Figure B 1-25-79) a complete ECG (only leads 11 and V₁ are shown in Figure 1 B) fails to show any artifacts when hiccups are absent.

Minutiae may carry significance in electrocardiography!



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UPR School of Medicine
Dept. of Medicine
Río Piedras, P. R. 00936

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CASE PRESENTATION

Thirty-six year old white male who was in his usual state of health until 4 months prior to his initial evaluation in 1976, when he started to complain of palpitations. There is no history of smoking, drinking or excessive caffeine intake. Holter electrocardiographic recording revealed frequent unifocal PVC's (15 PVC per hour). Routine laboratory work-up (CBC, SMA-18, chest x-ray, EKG, T3 & T4) was unremarkable. Physical examination revealed an S₄, there were no murmurs.

A. At this time you would:

- a. start anti-arrhythmic therapy with quinidine
- b. start anti-arrhythmic therapy with procainamide (Pronestyl)
- c. start anti-arrhythmic therapy with Disopyramide (Norpace)
- d. observe the patient in the CCU and start IV xylocaine

After anti-arrhythmic therapy was started, the patient improved. However, on a follow-up visit, a routine electrocardiographic tracing revealed premature ventricular contractions. Holter electrocardiographic recording showed frequent PVC, over 15 per hour.

B. At this time you would:

- a. measure the coupling interval of the PVC and compare with the coupling interval before anti-arrhythmic therapy was started.
- b. increase dose of anti-arrhythmic agent
- c. determine anti-arrhythmic drug serum levels
- d. add another anti-arrhythmic agent

The patient moved to another city in 1979 and subsequently discontinued all medications. He did well for 6 months until two hours prior to admission when he developed blurred vision, dizzy spells and diaphoresis. Electrocardiogram showed repeated bouts of ventricular tachycardia as well as frequent multifocal PVC's.

C. The treatment of choice would be:

- a. intravenous xylocaine 1 mg/Kg followed by 2-4 mg/min. IV
- b. intravenous procainamide 5 mg/Kg

- c. intravenous Bretylium 5 mg/Kg
- d. electrical cardioversion.

After IV anti-arrhythmic therapy he maintained sinus rhythm. Serial electrocardiographic enzyme determinations were normal. He was transferred to the ward on quinidine 300 mg q6hrs and phenobarbital 1/2 gr tid. Occasional PVC's were recorded. Serum quinidine levels were reported as 1.5 nonogram/cc. In view of the serum quinidine level below therapeutic range, the dose was increased to 400 mg qid. Phenobarbital was discontinued. Four days after discharge from the hospital, he developed a syncopal episode. No GI symptoms were reported prior to the syncopal episode.

D. The most likely explanation for the syncopal episode is:

- a. hypotension 2nd to alpha receptor blockade produced by quinidine
- b. cerebral embolism
- c. ventricular tachycardia
- d. drug interaction
- e. quinidine syncope

After he was brought to the Emergency Room, the BP was 110/80, the examination of the lungs and cardiovascular system were unremarkable. The electrocardiographic tracing most likely revealed:

- E.
- a. ventricular tachycardia
 - b. frequent PVC's
 - c. prolonged QT interval

At this time, what would be your approach to clarify the patient's medical problems?

- a. observe for 3-4 hrs, send him home or anti-arrhythmic therapy
- b. admit to CCU, order serum quinidine levels, continue quinidine p.o.
- c. admit to CCU, d/c quinidine, order serum quinidine level
- d. after an adequate period of observation, recommend exercise testing and if needed, coronary arteriography.

*** C O N T E S T A C I O N E S ***

A _____

B _____

C _____

D _____

E _____

Favor de contestar las preguntas y enviar respuesta a: Junta Editora, Asociación Médica de Puerto Rico, Apartado 9387, Santurce, P. R. 00908.

Al recibir sus contestaciones la Junta Editora o uno de nuestros consultores en enfermedades cardiovasculares se comunicará con usted para discutir el manejo del caso presentado.

J. M. Aranda, MD
Editor



Tail of whipworm
(*Trichuris trichiura*)

Vermox[®]: the only anthelmintic highly effective against whipworm.

	Cure Rate	Egg Reduction
VERMOX [®]	68%*	93%**
Mintezol ¹	35%†	45%††
Antiminth ²	Not Indicated	
Povan ³	Not Indicated	

Also highly effective against roundworm and hookworm

Since whipworm, roundworm and hookworm are all soil-borne helminths, mixed infections are not uncommon. Only one anthelmintic exhibits high efficacy rates for all three nematodes: whipworm—68%; roundworm—98%; hookworm—96%. That agent is VERMOX.[®]

Please see following page for Summary of Prescribing Information.

**Broad-spectrum coverage
in mixed helminthic infections**

Vermox[®] TABLETS
(mebendazole)



JANSSEN PHARMACEUTICA INC.
New Brunswick, N.J. 08903

*Committed to research...
because so much remains to be done.*

© 1981 Janssen Pharmaceutica, Inc.

JPI-023



**Broad-spectrum
coverage in mixed
helminthic infections**

Vermax[®]
(mebendazole)
TABLETS

Contraindications VERMOX is contraindicated in pregnant women (see: Pregnancy Precautions) and in persons who have shown hypersensitivity to the drug.

Precautions PREGNANCY: VERMOX has shown embryotoxic and teratogenic activity in pregnant rats at single oral doses as low as 10 mg/kg. Since VERMOX may have a risk of producing fetal damage if administered during pregnancy, it is contraindicated in pregnant women.

PEDIATRIC USE: The drug has not been extensively studied in children under two years; therefore, in the treatment of children under two years the relative benefit/risk should be considered.

Adverse Reactions Transient symptoms of abdominal pain and diarrhea have occurred in cases of massive infection and expulsion of worms.

Dosage and Administration The same dosage schedule applies to children and adults. The tablet may be chewed, swallowed or crushed and mixed with food. For the control of pinworm (enterobiasis), a single tablet is administered orally, one time.

For the control of roundworm (ascariasis), whipworm (trichuriasis), and hookworm infection, one tablet of VERMOX is administered, orally, morning and evening, on three consecutive days.

If the patient is not cured three weeks after treatment, a second course of treatment is advised. No special procedures, such as fasting or purging, are required.

* Mean cure rate of VERMOX[®] in treating whipworm; cure rate range of 61-75%. Data on file at Janssen Pharmaceutica Inc.

** Mean egg reduction of VERMOX[®] in treating whipworm; egg reduction range of 70-99%. Data on file at Janssen Pharmaceutica Inc.

† Rollo, I.M.: Drugs used in the chemotherapy of helminthiasis, in Goodman, L.S.; and Gilman, A. (eds.): *The Pharmacological Basis of Therapeutics*, ed. 5. New York, Macmillan, 1975, p. 1034.

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1. Registered trademark of Merck Sharp and Dohme.
2. Registered trademark of Roerig.
3. Registered trademark of Parke-Davis.



JANSSEN PHARMACEUTICA INC.
New Brunswick, N.J. 08903

*Committed to research...
because so much remains to be done.*

AVISO DE INTERES

La Junta Editora, consciente de su responsabilidad de hacer que el "Boletín" cumpla a cabalidad con su cometido de divulgar conocimientos médicos, elevar las normas de educación médica y al propio tiempo de llenar las necesidades de todos los compañeros médicos, ha acordado establecer una nueva Sección que se conocerá como "Sección de Preguntas".

Bajo esta nueva Sección, todos los compañeros tendrán la oportunidad de enviarnos preguntas médicas de casos difíciles o casos clínicos para opinión experta. Estas preguntas, con sus respuestas, serán publicadas en esta nueva Sección.

Las preguntas deberán ser enviadas a:

Boletín de la AMPR
Sección de Preguntas
Apartado 9387
Santurce, P. R. 00908

Esperamos sus preguntas.

Juan M. Aranda, MD
Presidente
Junta Editora

ROCHE

For recurrent attacks of urinary tract infection in women

Bactrim™ DS Double Strength Tablets

Each tablet contains 160 mg trimethoprim and 800 mg sulfamethoxazole.

Just one tablet b.i.d. for 10 to 14 days



- Action at urinary/vaginal/lower bowel sites helps eliminate reservoirs of infecting organisms
- Distinctive antibacterial action plus wide spectrum helps eradicate recurrent UTI
- Low incidence of bacterial resistance in community practice

- Convenient b.i.d. dosage provides day-and-night antibacterial control
- Contraindicated during pregnancy and the nursing period. During therapy, maintain adequate fluid intake; perform CBC's and urinalyses with microscopic examination.

Before prescribing, please consult complete product information, a summary of which follows:

Indications and Usage: For the treatment of urinary tract infections due to susceptible strains of the following organisms: *Escherichia coli*, *Klebsiella-Enterobacter*, *Proteus mirabilis*, *Proteus vulgaris*, *Proteus morganii*. It is recommended that initial episodes of uncomplicated urinary tract infections be treated with a single effective antibacterial agent rather than the combination. Note: The increasing frequency of resistant organisms limits the usefulness of all antibacterials, especially in these urinary tract infections.

Also for the treatment of documented *Pneumocystis carinii* pneumonitis. To date, this drug has been tested only in patients 9 months to 16 years of age who were immunosuppressed by cancer therapy.

The recommended quantitative disc susceptibility method (Federal Register, 37:20527-20529, 1972) may be used to estimate bacterial susceptibility to Bactrim. A laboratory report of "Susceptible to trimethoprim-sulfamethoxazole" indicates an infection likely to respond to Bactrim therapy. If infection is confined to the urine, "Intermediate susceptibility" also indicates a likely response. "Resistant" indicates that response is unlikely.

Contraindications: Hypersensitivity to trimethoprim or sulfonamides; pregnancy; nursing mothers; infants less than two months of age.

Warnings: Deaths from hypersensitivity reactions, agranulocytosis, aplastic anemia and other blood dyscrasias have been associated with sulfonamides. Experience with trimethoprim is much more limited but occasional interference with hematopoiesis has been reported as well as an increased incidence of thrombopenia with purpura in elderly patients on certain diuretics, primarily thiazides. Sore throat, fever, pallor, purpura or jaundice may be early signs of serious blood disorders. Frequent CBC's are recommended; therapy should be discontinued if a significantly reduced count of any formed blood element is noted.

Precautions: Use cautiously in patients with impaired renal or hepatic function, possible folate deficiency, severe allergy or bronchial asthma. In patients with glucose-6-phosphate dehydrogenase deficiency, hemolysis, frequently dose-related, may occur. During therapy, maintain adequate fluid intake and perform frequent urinalyses, with careful microscopic examination, and renal function tests, particularly where there is impaired renal function.

Adverse Reactions: All major reactions to sulfonamides and trimethoprim are included, even if not reported with Bactrim. **Blood dyscrasias:** Agranulocytosis, aplastic anemia, megaloblastic anemia, thrombopenia, leukopenia, hemolytic anemia, purpura, hypoprothrombinemia and methemoglobinemia. **Allergic reactions:** Erythema multiforme, Stevens-Johnson syndrome, generalized skin eruptions, epidermal necrolysis, urticaria, serum sickness, pruritus, exfoliative dermatitis, anaphylactoid reactions, periorbital edema, conjunctival and scleral injection, photosensitization, arthralgia and allergic myocarditis. **Gastrointestinal reactions:** Glossitis, stomatitis, nausea, emesis, abdominal pains, hepatitis, diarrhea and pancreatitis. **CNS reactions:** Headache,

peripheral neuritis, mental depression, convulsions, ataxia, hallucinations, tinnitus, vertigo, insomnia, apathy, fatigue, muscle weakness and nervousness. **Miscellaneous reactions:** Drug fever, chills, toxic nephrosis with oliguria and anuria, periarteritis nodosa and L. E. phenomenon. Due to certain chemical similarities to some goitrogens, diuretics (acetazolamide, thiazides) and oral hypoglycemic agents, sulfonamides have caused rare instances of goiter production, diuresis and hypoglycemia in patients; cross-sensitivity with these agents may exist. In rats, long-term therapy with sulfonamides has produced thyroid malignancies.

Dosage: Not recommended for infants less than two months of age.

Urinary Tract Infections: Usual adult dosage—1 DS tablet (double strength), 2 tablets (single strength) or 4 teasp. (20 ml) b.i.d. for 10-14 days.

Recommended dosage for children—8 mg/kg trimethoprim and 40 mg/kg sulfamethoxazole per 24 hours, in two divided doses for 10 days. A guide follows:

Children two months of age or older

Weight		Dose—every 12 hours	
lbs	kgs	Teaspoonfuls	Tablets
20	9	1 teasp. (5 ml)	½ tablet
40	18	2 teasp. (10 ml)	1 tablet
60	27	3 teasp. (15 ml)	1½ tablets
80	36	4 teasp. (20 ml)	2 tablets or 1 DS tablet

For patients with renal impairment:

Creatinine Clearance (ml/min)	Recommended Dosage Regimen
Above 30	Usual standard regimen
15-30	½ the usual regimen
Below 15	Use not recommended

***Pneumocystis carinii* pneumonitis:** Recommended dosage: 20 mg/kg trimethoprim and 100 mg/kg sulfamethoxazole per 24 hours in equal doses every 6 hours for 14 days. See complete product information for suggested children's dosage table.

Supplied: Double Strength (DS) tablets, each containing 160 mg trimethoprim and 800 mg sulfamethoxazole, bottles of 100; Tel-E-Dose® packages of 100 Tablets, each containing 80 mg trimethoprim and 400 mg sulfamethoxazole—bottles of 100 and 500; Tel-E-Dose® packages of 100; Prescription Paks of 40, available singly and in trays of 10. Oral suspension, containing in each teaspoonful (5 ml) the equivalent of 40 mg trimethoprim and 200 mg sulfamethoxazole, fruit-licorice flavored—bottles of 16 oz (1 pint).

ROCHE

Roche Laboratories
Division of Hoffmann-La Roche Inc.
Nutley, New Jersey 07110

Please see back cover.

Her next attack of cystitis may require

the Bactrim 3-system counterattack



ROCHE

Bactrim has shown high clinical effectiveness in recurrent cystitis as a result of its wide spectrum and distinctive antimicrobial action in the urinary, vaginal and lower intestinal tracts.

The probability of recurrent urinary tract infection appears to be enhanced by the establishment of large numbers of *E. coli* or other urinary pathogens on the vaginal introitus. The trimethoprim component of

Bactrim diffuses into vaginal fluid in effective concentrations, thus combating migration of pathogens into the urethra.

Studies have shown that Bactrim acts against *Enterobacteriaceae* in the bowel without the emergence of resistant organisms. Thus, Bactrim reduces the risk of introital colonization by fecal uropathogens. It has *no* significant effect on other normal, necessary intestinal flora.

Bactrim fights uropathogens in the urinary tract/vaginal tract/lower intestinal tract

Please see reverse side for summary of product information.



BOLETIN

ASOCIACION MEDICA DE PUERTO RICO

CONTENIDO:

SURGICAL TREATMENT OF TOTAL OCCLUSION OF LEFT CORONARY
ARTERY AND SIGNIFICANT STENOSIS OF RIGHT CORONARY ARTERY

THE SUPERIOR VENA CAVA SYNDROME: AN ONCOLOGIC EMERGENCY

NOCARDIOSIS PULMONAR
PRESENTACION DE UN CASO Y REPASO DE LA LITERATURA

EDITORIAL

LENGUA Y MEDICINA

LA PROFESION Y EL MAL USO DEL IDIOMA ESPAÑOL

PONENCIA SOBRE LENGUA Y MEDICINA — "EL REMEDIO AL PROBLEMA"

GRAPHICS — "MYCOSIS FUNGOIDES"

MEDI-QUIZ

ABSTRACTOS — CURSOS — NOTICIAS

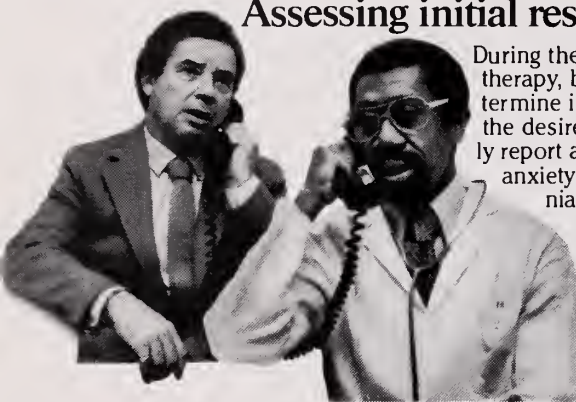
EKG OF THE MONTH

INDICE PAGINA 163

COLLEGE OF MEDICINE
BOSTON
JUL 22 1980

Monitoring patient response to Valium® (diazepam/Roche)

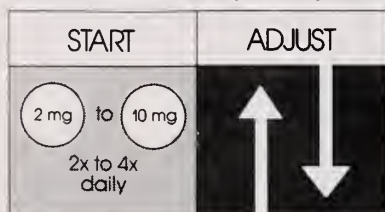
Assessing initial response to therapy



During the first follow-up visit after initiating therapy, both physician and patient should determine if Valium (diazepam/Roche) is having the desired effect. Most patients will promptly report a feeling of relaxation and relief of anxiety-linked symptoms such as insomnia, headaches, palpitations and hyperventilation. You will probably observe that the patient is calmer and more relaxed. If, however, patient response does not measure up to expectations, a reevaluation of the patient's profile with modification of the dosage regimen should be considered.



Making dosage adjustments



With any psychoactive medication it is good medical practice to initiate therapy at base dosage levels and titrate to the patient's needs. With Valium, experience has shown that 5 mg t.i.d. is usually sufficient although some patients with severe or persistent anxiety may require higher dosages initially. In geriatric or debilitated patients, the recommended dosage is 2 to 2 1/2 mg once or twice daily.

When anxiety fluctuates, as is common with most patients, the dosage may be adjusted as needed during the course of therapy; three strengths in scored tablets give you unmatched flexibility and simplicity in individualizing dosage.

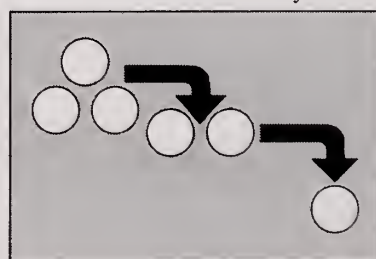
Evaluating progress toward therapeutic goals

SET GOALS						
		1	2	3	4	5
6	7	8	9	10	11	12
13	14	15	16	17	18	19
20	21	22	23	24	25	26
27	28	29	30	31		

At the beginning of therapy it is now common practice for both physician and patient to establish treatment goals and to estimate the amount of time needed to achieve them. Then the patient knows what to expect and when to expect it.

Some physicians find that compiling a checklist of presenting symptoms and complaints is useful for assessing the patient's response from visit to visit. In this way, progress toward attainment of the therapeutic goal is reviewed at regular intervals. As patients feel their symptoms abate and begin to develop insight into the sources of their anxiety and psychic tension, the checklist can be expected to dwindle.

Discontinuing pharmacologic intervention



When you decide to discontinue therapy, tapering dosage is good medical practice. Although rarely necessary after short-term treatment with Valium, gradual dosage reduction is advisable for patients who have been on extended therapy. This gradual discontinuance should preclude either recurrence of pretreatment symptoms or development of untoward side effects. Symptoms of withdrawal have almost always been associated with abrupt discontinuance of therapy at higher dosages taken continuously over long periods of time.

2-mg, 5-mg, 10-mg scored tablets
Valium®
diazepam/Roche

An Important Adjunct to Your Treatment
Program for Excessive Anxiety



See the following page for a summary of product information.

Valium® (diazepam/Roche) ®

Before prescribing, please consult complete product information, a summary of which follows:

Indications: Tension and anxiety associated with anxiety disorders, transient situational disturbances and functional or organic disorders; psychoneurotic states manifested by tension, anxiety, apprehension, fatigue, depressive symptoms or agitation; symptomatic relief of acute agitation, tremor, delirium tremens and hallucinosis due to acute alcohol withdrawal; adjunctively in skeletal muscle spasm due to reflex spasm to local pathology; spasticity caused by upper motor neuron disorders; atetosis, stiff-man syndrome, convulsive disorders (not for sole therapy).

The effectiveness of Valium (diazepam/Roche) in long-term use, that is, more than 4 months, has not been assessed by systematic clinical studies. The physician should periodically reassess the usefulness of the drug for the individual patient.

Contraindicated: Known hypersensitivity to the drug. Children under 6 months of age. Acute narrow angle glaucoma, may be used in patients with open angle glaucoma who are receiving appropriate therapy.

Warnings: Not of value in psychotic patients. Caution against hazardous occupations requiring complete mental alertness. When used adjunctively in convulsive disorders, possibility of increase in frequency and/or severity of grand mal seizures may require increased dosage of standard anticonvulsant medication; abrupt withdrawal may be associated with temporary increase in frequency and/or severity of seizures. Advise against simultaneous ingestion of alcohol and other CNS depressants. Withdrawal symptoms similar to those with barbiturates and alcohol have been observed with abrupt discontinuation, usually limited to extended use and excessive doses. Infrequently, milder withdrawal symptoms have been reported following abrupt discontinuation of benzodiazepines after continuous use, generally at higher therapeutic levels, for at least several months. After extended therapy, gradually taper dosage. Keep addiction-prone individuals under careful surveillance because of their predisposition to habituation and dependence.

Usage in Pregnancy: Use of minor tranquilizers during first trimester should almost always be avoided because of increased risk of congenital malformations as suggested in several studies. Consider possibility of pregnancy when instituting therapy; advise patients to discuss therapy if they intend to or do become pregnant.

Precautions: If combined with other psychotropics or anticonvulsants, consider carefully pharmacology of agents employed, drugs such as phenothiazines, narcotics, barbiturates, MAO inhibitors and other antidepressants may potentiate its action. Usual precautions indicated in patients severely depressed, or with latent depression, or with suicidal tendencies. Observe usual precautions in impaired renal or hepatic function. Limit dosage to smallest effective amount in elderly and debilitated to preclude ataxia or oversedation.

Side Effects: Drowsiness, confusion, diplopia, hypotension, changes in libido, nausea, fatigue, depression, dysarthria, jaundice, skin rash, ataxia, constipation, headache, incontinence, changes in salivation, slurred speech, tremor, vertigo, urinary retention, blurred vision. Paradoxical reactions such as acute hyperexcited states, anxiety, hallucinations, increased muscle spasticity, insomnia, rage, sleep disturbances, stimulation have been reported, should these occur, discontinue drug. Isolated reports of neutropenia, jaundice, periodic blood counts and liver function tests advisable during long-term therapy.

Dosage: Individualize for maximum beneficial effect. **Adults:** Tension, anxiety and psychoneurotic states, 2 to 10 mg b.i.d. to q.i.d.; alcoholism, 10 mg t.i.d. or q.i.d. in first 24 hours, then 5 mg t.i.d. or q.i.d. as needed, adjunctively in skeletal muscle spasm, 2 to 10 mg t.i.d. or q.i.d., adjunctively in convulsive disorders, 2 to 10 mg b.i.d. to q.i.d. **Geriatric or debilitated patients:** 2 to 2½ mg, 1 or 2 times daily initially, increasing as needed and tolerated. (See Precautions.) **Children:** 1 to 2½ mg t.i.d. or q.i.d. initially, increasing as needed and tolerated (not for use under 6 months).

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Tobin JM et al: *Geriatrics* 25(6):122, 1970.

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- * **Surgical Treatment of Total Occlusion of Left Coronary Artery and Significant Stenosis of Right Coronary Artery** 163
Jorge O. Just Viera, MD

In this issue, Dr. Just Viera describes the medical and surgical management of a 48-year old male with total occlusion of the left coronary artery and significant lesions in the right coronary artery. He had developed angina pectoris and a subendocardial infarction prior to cardiac catheterization.

Although an exercise test was not performed, this dynamic test might have revealed evidence indicative (significant depression of the ST segment) of severe obstructive coronary artery disease.

In a patient with stable angina pectoris, significant depression of the ST segment (> 2 mm) in the early stages of a gradual exercise test, is an indication for angiographic studies.

- * **The Superior Vena Cava Syndrome: An Oncologic Emergency** 168
*Antonio A. Ydrach, MD, FACP, Víctor A. Marcial, MD, FACR and
Nayda Figueroa Valles, MD*

Ydrach et al present and discuss the clinical features of the superior vena cava syndrome. This syndrome is usually secondary to carcinoma of the lung or lymphoma, however other conditions such as an intrathoracic goiter, syphilitic aneurysm, constrictive pericarditis and fibrosing mediastinitis can produce it. The authors emphasize the medical and therapeutic approach to this oncologic emergency. An interesting observation is the use of of radioactive venography as a diagnostic tool in this condition. It is atraumatic with a low morbidity rate. Although some investigators have used chemotherapy to treat this oncologic emergency, Ydrach presents a rather complete review of the literature which favors radiotherapy as the treatment of choice. Excellent article which should be of interest to all.

- * **Nocardiosis Pulmonar - Presentación de un Caso y Repaso de la Literatura** 174
Rafael Quiñones, MD, Guillermo J. Vázquez, MD y Carlos H. Ramírez Ronda, MD

Quiñones y colaboradores presentan en esta edición, un paciente con nocardiosis pulmonar. Enfatizan los autores que la única manera de diagnosticar esta condición es recordando que todo paciente, especialmente el inmunocomprometido con envolvimento pulmonar, cerebral o cutáneo puede estar padeciendo de esta infección. Nocardia no es un oportunista común de las vías respiratorias superiores ni tampoco es un contaminante habitual del laboratorio. Es por estas razones que todo paciente en el cual se aísle Nocardia en esputo, debe de considerarse un hallazgo patológico importante que amerita confirmación inmediata. La discusión del caso y la revisión de la literatura serán de gran interés para todos los lectores.

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SURGICAL TREATMENT OF TOTAL OCCLUSION OF LEFT CORONARY ARTERY AND SIGNIFICANT STENOSIS OF RIGHT CORONARY ARTERY

Jorge O. Just Viera, MD

Abstract: Total occlusion of the left main coronary artery combined with significant segmental occlusion of the right coronary artery was demonstrated angiographically in a 48-year old active minister. He underwent triple coronary artery bypass successfully. Diastolic augmentation with intra-aortic balloon pumping during induction and surgery was used. He recovered rapidly from surgery, returned to work in 6 weeks and has remained well for the last year. This lesion may be more frequent than realized and should be treated surgically.

Abstracto: Se presenta un caso de oclusión total de la coronaria izquierda combinado con oclusión significativa (> 75 por ciento) en la coronaria derecha en un hombre de 48 años de edad. El paciente se operó, recibiendo tres puentes aorto-coronarios sin complicaciones operatorias. Esta lesión parece ser más frecuente de lo que se pensaba y debe ser tratada quirúrgicamente en todos los casos donde se establece el diagnóstico.

Survival from total occlusion of the

From the Cardiovascular Center, Mercy-Memorial Hospitals, Benton Harbor, Michigan.

left coronary artery is rare. This lesion is related to sudden death, and surgical intervention has been infrequent. Crosby (1) and his group reviewed 13 patients with total occlusion of the left coronary artery previously reported in the literature. Seven had surgical treatment. These authors added 4 surgically treated patients and brought to 11 the total number of patients treated by surgery.

A patient with total occlusion of the left coronary artery combined with significant stenosis of the right coronary artery was successfully operated recently. This lesion may be more common than realized, which justifies this report.

I - Case Report: K. B., Mercy Hospital No. 164499-6

This 48 year old white minister was referred for elective open heart surgery. He claimed good health until approximately six months prior to admission. During that time he had infrequent chest pains on activity. As a minister he climbed stairs, often, to visit patients in different areas of the hospital. Symptoms of substernal or lateral chest discomfort and burning gave him no concern. Approximately three months prior to his heart surgery, he was admitted to Memorial Hospital, Saint Joseph, Michigan, with an acute myocardial infarction. At that time, serial CPK enzyme determinations rose to 280 with significant increase of fraction 2. The electrocardiogram demonstrated only ST segment depression without

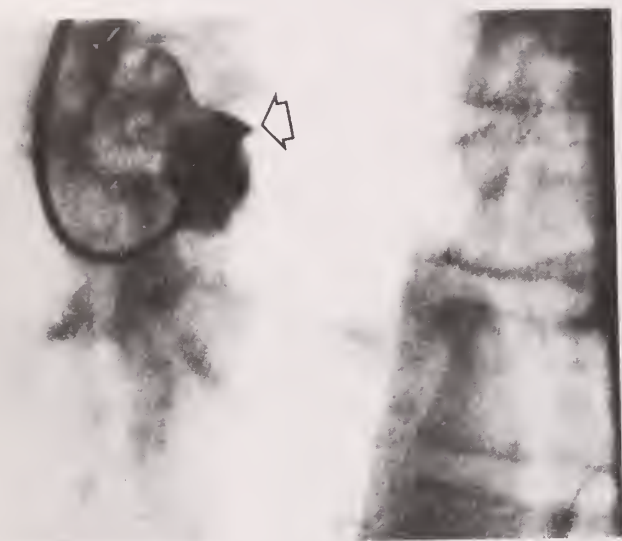


Figure 1: Total occlusion of the left main coronary artery just beyond its origin is demonstrated.

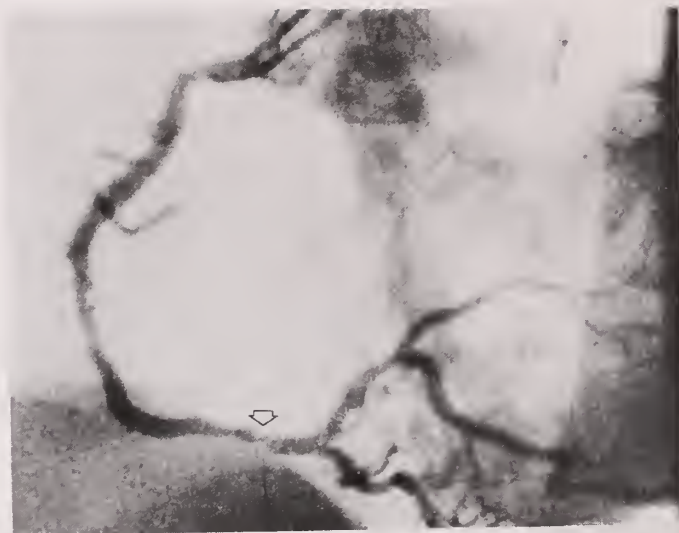


Figure 2: A significant stenosis is shown in the right coronary artery just proximal to its bifurcation.

any evidence of acute transmural infarct. He was stable clinically and was referred for coronary angiography. This study was carried out in July, 1978, without difficulty except for temporary mild hypotension treated with Aramine intravenously. The coronary angiogram demonstrated total occlusion of the left main coronary artery just beyond its origin. (Figure 1). The right coronary artery was dominant and had a 75 percent segmental stenosis about 1 to 1.5 centimeters prior to its bifurcation with diffuse irregularity proximally. (Figure 2) Numerous septal branches were seen as well as collaterals to the circumflex. The diagonal vessel appeared to be larger than the anterior descending, and the anterior descending was visualized in interrupted segments and could not be demonstrated throughout its whole length. The collaterals filled the left coronary artery up to the left main stem at which point complete occlusion was demonstrated again retrogradely. (Figure 3) The ventriculogram showed diffuse marked hypokinesis improved by Nitroglycerine, most effective at the dia-

phragmatic wall. (Figure 4) The left ventricular end diastolic pressure was 15 mm Hg. Because of the recent history of myocardial infarction, it was elected to wait before surgical intervention and the patient was kept at minimal activity.

The patient was taken to the operation room on August 2, 1978. The intra-aortic balloon was inserted under local anesthesia. When the left femoral artery was opened, a recent thrombus was found and removed. Histologic analysis did not reveal tumor cells. These were atherosclerotic plaques in the femoral artery, but these were not disturbed when the balloon pump was inserted.

The patient was then anesthetized with diastolic augmentation. The blood pressure did not vary. The heart was exposed and plaques were observed and palpated in the wall of the left anterior descending coronary artery at the junction of its middle and distal third, consistent with the angiographic demonstration of streaming at this point. Disease was evident in the wall of the proximal diagonal and circumflex



Figure 3: Collaterals are demonstrated filling retrogradely the distal circumflex, anterior descending and diagonal coronary arteries.

arteries and palpation at the base of the heart revealed a very prominent calcific density in the left main coronary artery. The heart contracted sluggishly, especially the anterior wall.

Cardiopulmonary bypass with systemic hypothermia to 25°C was utilized with intermittent aortic clamping. The heart was retracted outside the chest and the circumflex coronary artery was approached at the atrioventricular groove. Utilizing 7-0 Mersilene, an end to-side anastomosis was made between the previously harvested saphenous vein and the circumflex. The vein was passed behind the aortic root through the transverse sinus and anastomosed to the lateral part of the aortic root. The heart was then allowed to fall back into the chest and the left anterior descending was entered just before its division into terminal and diagonal branches. A cobra shaped end to-side anastomosis between vein and coronary artery was made. The vein was curved over the pulmonary artery and anastomosed to the lateral side of the aortic root.

Circulation was restored to the left side pending anastomosis to the right coronary artery. The heart was retracted to the left, exposing the right coronary artery, which was dissected until the bifurcation was

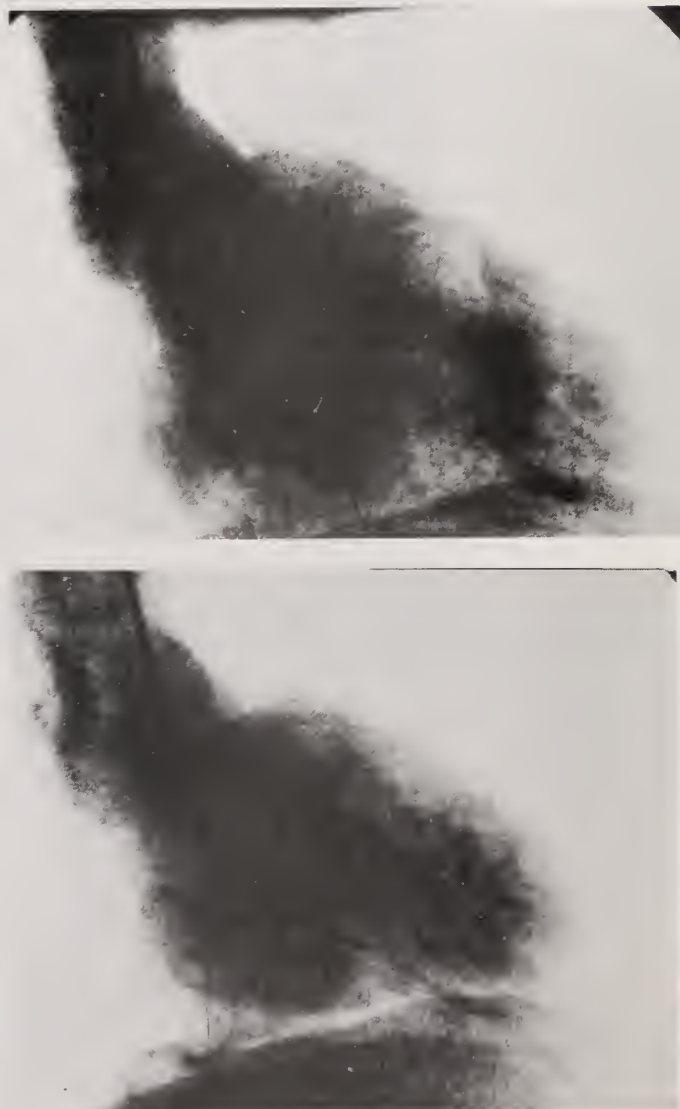


Figure 4: A) Ventriculogram shows generalized hypokinesia which improved with administration of nitroglycerine, as can be appreciated in (B).

demonstrated clearly. It was entered just prior to the bifurcation and the vein was anastomosed to the right coronary artery with 7-0 Mersilene, and subsequently to the mid portion of the aortic root. During the time the aorta was clamped for anastomosis of the vein to the right coronary artery, perfusion occurred through the other grafts to the left side.

The patient was rewarmed and the heart was

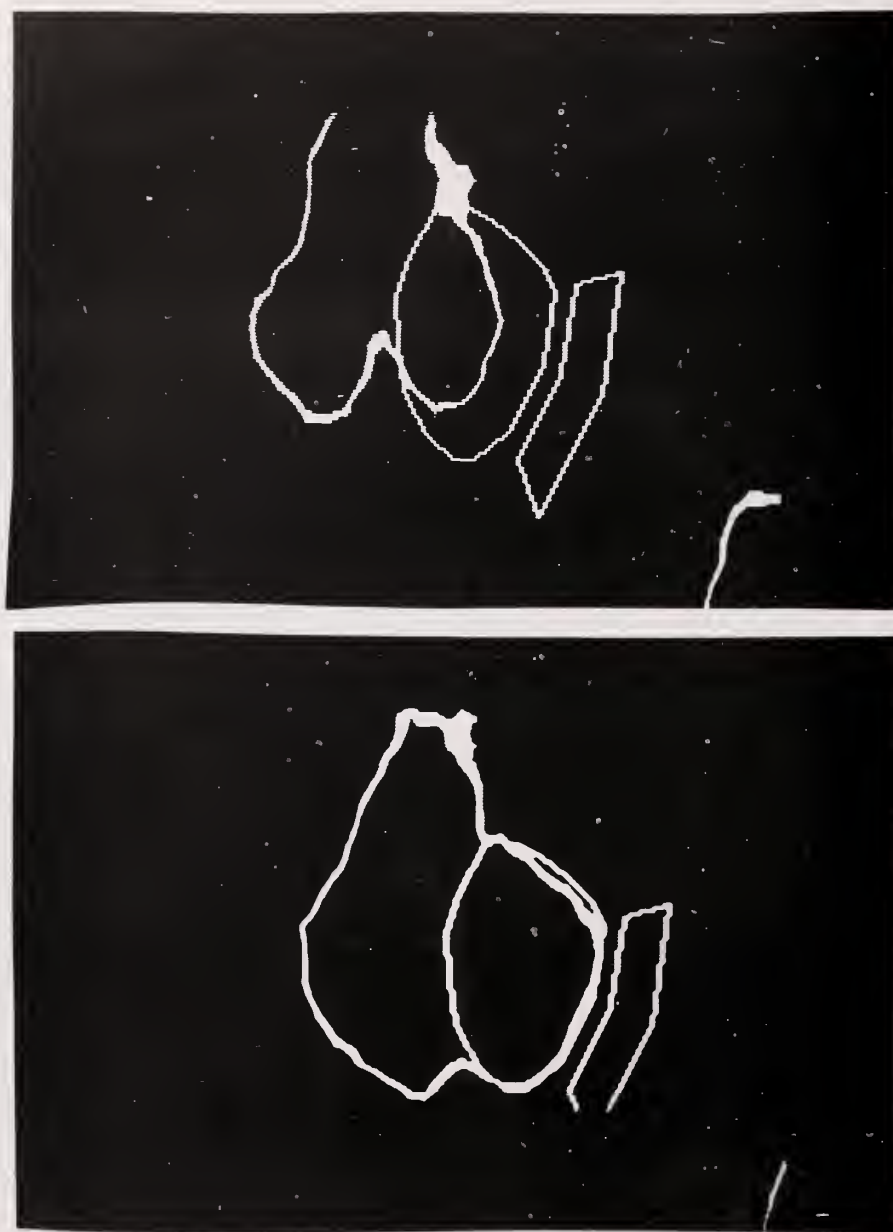


Figure 5: Outline of left ventricle by cardiac radionuclide angiogram in systole (A) and diastole (B) performed after surgery and estimated to be in the lower limits of normal.

defibrillated at 30°C. One one occasion it went into atrial fibrillation with a rapid ventricular response and this was treated electrically. Cardiopulmonary bypass was discontinued without difficulty, the heart contracted well and resumed sinus rhythm. During this time the intra-aortic balloon pump had been set

on a 1 to 1 ratio. After hemodynamic stability, the ratio was changed to 2 to 1, and then 4 to 1. It was decided to remove the balloon pump because he appeared to be doing very well. Since the atherosclerotic plaques in the left leg required correction, the chest remained open during the removal of the balloon pump

for ready access if needed.

A plaque totally occluded the orifice of the superficial femoral artery and covered about 60 percent of the profunda femoral orifice. The arterial incision was extended into the distal superficial femoral and an endarterectomy was then performed. Good back flow was established from both superficial and profunda femoral arteries. A patch of Dacron enlarged the lumen. The chest was then closed along with the extremity incisions.

The patient had an uneventful postoperative course. He received two units of whole blood but did not have any further need for volume replacement. He was transferred from the Intensive Care Unit to the ward in 48 hours, where he started an exercise program which he tolerated well. He was discharged on the 10th postoperative day.

During the first month, he increased his activity gradually and four weeks after surgery was walking one mile three times a day. He returned to work 6 weeks after surgery and has remained active and asymptomatic. On April 25, 1979 a cardiac radionuclide angiogram was performed which demonstrated good ventricular function with an ejection fraction calculated to be in the lower limits of normal.

Discussion

Crosby and co-workers (1) described the incidence of total occlusion of the left main coronary artery as being 0.76 percent of all patients undergoing coronary revascularization. The incidence found in their cardiac laboratory was 0.17 percent.

At Mercy Hospital, Benton Harbor, Michigan, this is the first case observed in 2403 cardiac catheterizations and 304 surgical procedures for an incidence of 0.04 percent and 0.3 percent respectively.

Crosby and co-workers added their four patients, all treated surgically, to the 13

patients reported previously in the literature. Six patients were treated medically, with a follow up of four months to seven years. Of these, three died and three survived. Eleven patients were treated surgically. Ten survived and were followed from 3 months to 5.5 years. One patient died after single vessel revascularization three days postoperatively.

Three of four patients treated by Crosby and his group had additional occlusions of the right coronary artery of more than 50 percent and the left ventricular function was from very poor to moderate. Two of his patients were treated with insertion of the intra-aortic balloon pump before anesthesia and two were treated without this support.

In contrast, our patient had very little symptoms and had had evidence of a non-transmural infarct. The paucity of his symptoms is worrisome since the serious combination of total occlusion of the left coronary artery and significant stenosis of the right coronary artery may be more frequent than thought previously. Prompt surgical intervention is recommended without undue consideration of the presence or absence of symptoms.

Acknowledgments

William Rock, M. D., Family Practitioner, and Benjamin Son, M. D., Cardiologist, kindly referred this patient for surgery.

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1. Crosby, I. K., Wellons, H. A. and Burwell, L.: Total Occlusion of Left Coronary Artery, Incidence and Management, J. Thora. Cardiovasc. Surg. 77: 389-391, 1979.

THE SUPERIOR VENA CAVA SYNDROME: AN ONCOLOGIC EMERGENCY

Arturo A. Ydrach, MD, FACP, Víctor A. Marcial, MD, FACR and
Nayda Figueroa Valles, MD

Summary: A case recently seen by us at the Puerto Rico Medical Center with the superior vena cava syndrome due to carcinoma of the lung is presented. The etiology, pathophysiology, diagnosis and treatment controversies are reviewed. We are treating the superior vena cava syndrome with relative frequency, and find management is often delayed in searching for a histologic diagnosis. Palliation can often be obtained with radiotherapy alone. Our experience with 7 cases seen from 1977-1979 is also presented.

Resumen: Presentamos un caso tratado por nosotros recientemente con el síndrome de vena cava superior debido a carcinoma de pulmón, la causa más común al presente. Repasamos la patofisiología, el diagnóstico y manejo de esta emergencia oncológica que vemos con relativa frecuencia en el Hospital Universitario del Centro Médico de Puerto Rico. Encontramos que muchas veces se demora el tratamiento al exigir siempre un diagnóstico histológico. Se repasa la experiencia de 7 casos tratados desde 1977-1979, y vemos que se puede obtener paliación con radioterapia.

From the P. R. Cancer Center, Department of Radiation Oncology, University of Puerto Rico, Medical Sciences Campus, San Juan, Puerto Rico.

Introduction

The superior vena cava syndrome is an oncologic emergency. It is usually the result of partial or complete occlusion of the S. V. C. by a malignant tumor. At present, carcinoma of the lung is the most common etiology, being the cause of the S. V. C. syndrome in 80-90 percent cases (5). Lymphoma is the second most common malignancy that causes the S. V. C. syndrome. As recently as 1954, about 40 percent of cases presenting with the superior vena cava syndrome were due to syphilitic aortitis causing a saccular aortic aneurysm and to fibrosing mediastinitis due to tuberculosis (8).

The S. V. C. syndrome was first described by William Hunter in 1775 in a patient with a syphilitic saccular aneurysm of the aorta. Even today about 3 percent of cases are still caused by benign conditions (1). Goiter extending intrathoracically is probably the most common benign cause of the superior vena cava syndrome, but idiopathic fibrosing mediastinitis and constrictive pericarditis can also cause the S. V. C. syndrome (3).

Since about 3 percent of cases of bronchogenic carcinoma result in the S. V. C. syndrome in some phase of its clinical course (5, 6), and since 776 cases (4) were reported by the Puerto Rico Cancer Registry to have bronchogenic carcinoma of the lung in 1974, 1975 and 1976, we would expect about 23 cases with the syndrome during those 36 mon-

ths from this cause alone in Puerto Rico.

The purpose of this paper is to present a case recently seen by us at the Puerto Rico Medical Center, and to review our experience with 6 other cases seen from 1977-1979 (Table I). Also the anatomic pathology, pathophysiology, diagnosis and management of this oncologic emergency will be reviewed.

Case Report and Presentation of Data

A 53 year old male, a chronic smoker, with dyspnea on exertion and chest pain of 5 months duration was admitted to the University District Hospital on 3-17-78. Three weeks prior to admission he developed edema of the face and neck. He also had orthopnea, severe shortness of breath, dyspnea on exertion, occasional lightheadedness, visual blackouts when reading, loss of appetite, hemoptysis and a 15 pound weight loss.

Physical examination showed swollen erythematous face and neck and distended neck veins. There were no palpable nodes and the trachea was in the midline. Chest X-ray showed a mediastinal mass and some right upper lobe atelectasis. On 3-20-78, fiberoptic bronchoscopy was done and showed a fungating, friable lesion obstructing the right upper lobe bronchus. The biopsy only showed atypical cells suspicious of squamous cell carcinoma.

Radiotherapy was started on the day of the biopsy with A-P and P-A fields, linear accelerator 8MEV X-rays, to include mediastinum and supraclavicular and hilar areas with 200 rad fractions, five times per wk.; after 400 rad daily for the first three days. The patient received 5,200 rad from 3-20-78 to 4-26-78.

On 4-3-78, repeat fiberoptic bronchoscopy was done, due to equivocal findings from the first procedure, and the biopsy showed squamous cell carcinoma.

At first follow-up, in 5-26-78, one month after the end of radiotherapy, the patient still had edema of the neck, dilated neck veins, and was still short of breath with exertion.

The patient died at home suddenly during an episode of severe shortness of breath, on 6-21-78.

Comments on the Case Report:

The survival of about 93 days from the date of admission to our hospital is very short. Furthermore, although total dose of radiotherapy to 5,200 rad was delivered, no significant palliation of the superior vena cava syndrome was achieved. Earlier treatment of cases prior to thrombosis of the superior vena cava produce more significant palliation with frequent reversal of edema and respiratory symptoms. A full course of radiotherapy in this case failed to change the clinical picture of edema of the face and the shortness of breath.

Presentation of Data

Our experience presented in Table I shows 7 cases seen by us at the Radiation Oncology Department of the University of P. R. Medical School from 1977 to 1979. Case No. 8 in Table I died prior to effective therapy 5 days after admission to the University Hospital.

The most common diagnosis was carcinoma of the lung in 6/8 (75 percent) of cases. One of the remaining, case number 8, was a non-Hodgkin's lymphoma diagnosed at autopsy. In case number 7, no diagnosis was obtained despite bilateral axillary node biopsies and mediastinal exploration after starting radiotherapy.

Palliation was obtained in our series in 2/6 (33 percent) of cases with carcinoma of the lung.

Survival was very poor in our patients with carcinoma of the lung, ranging from 6 days to 204 days after the diagnosis.

Discussion

Anatomically the superior vena cava is a 7 cm long, thin-walled, low pressure vessel in the right superior anterior mediastinum. It extends from the first costochondral car-

TABLE I
Cases with the Superior Vena Cava Syndrome at Radiotherapy Department
University District Hospital 1977-1979

Case No.	Age & Sex	Date Ist Seen	Symptoms	Signs	Radiological Studies	Histology	Method of Dx.	Treatment	Response Rx.	Comments and Survival
1	63 M	6/1/77	Hoarseness 7 mo.	edema face, neck and thorax	Chest X-rays: mediastinal mass, pleural effusion, sup. venocavogram bilateral obstruction both subclavian veins.	Undifferentiated small cell carcinoma	6/1/77 Bronchoscopy- Cytology of pleural effusion	400 rads x 3 200 rads daily to TD 1,800 rads.	Relief of symptoms but no decrease in mass. Died 14 days after diagnosis	Heavy smoker 14 d.
2	51 F	8/31/77	swelling of face neck and thorax increased collateral circulation acute respiratory distress on 9/28/77.		anterior mediastinal mass	anaplastic carcinoma of lung	pleural tap. 9/21/77	400 rads x 3 200 rads daily TD - 4,200 rads.	approx. 50 percent decrease in mass. Relief of symptoms.	Died - 4/15/78 204 d.
3	77 M	11/3/77	cough, anorexia weight loss	swelling of arms face and thorax since 2 mo. prior to admission supraclav. node.	Mediastinal mass anterior and middle mediastinum	Biopsy-poorly diff. squamous cell ca.	Biopsy of supraclavicular nodes. 11/16/77	400 rads x 3 TD - 1,200 rads	died - 11/22/77	Heavy smoker 6 d.
4	53 M	3/17/78	dyspnea, cough chest pain hemoptysis	swelling of face & neck, since 3 week prior to admission jugular vein distention	mediastinal mass	well diff. squamous cell carcinoma lung RUL	Bronchoscopy 3/20/78	400 rads x 3 200 rads daily TD - 5,200 rads	relief of symptoms no change in X-ray image-died 6/21/78	Heavy smoker (Patient in our case report) 93 days
5	60 M	2/7/79	chest pain hemoptysis weight loss anorexia	swelling of face and thorax	Right mediastinal mass	squamous cell carcinoma	cytology - squamous cell ca. well diff.	200 rads daily TD - 1,600 rads	Worsening symptoms. Died - 3/4/79	Heavy smoker 28 d.
6	62 M	3/19/79	Rt. arm and shoulder pain developed SVC syndrome	flushing of face and thorax increased collateral circulation.	Rt. hilar mass	poorly diff. squamous cell carcinoma	bronchoscopy- mass RUL 3/23/79	200 rads daily TD - 5,000 rads	complete relief of symptoms and signs	Heavy smoker last follow-up 9/9/79 Asymptomatic chest X-rays post radiation changes
7	28 M	9/14/79	shortness of breath	swelling of face and arms	negative chest X-ray positive S.V. cavogram	no histo. Dx.	axillary Bx(x2) mediastinal exploration	400 rads day No. 1 and 200 rads / d. TD - 2,000 rads Oct. 1-16/79	no response of edema or venous distension	Despite expl. thoracotomy no diagnosis made and radiotherapy interrupted at 2,000r.
8	34 M	July/79	shortness of breath			disseminated non-Hodgkin's lymphoma	Autopsy Dx.	None		died 5 days after admission

tilage to the upper border of the third costochondral cartilage to the right of the sternum. It is in close proximity to the trachea, sternum and right main stem bronchus. The superior vena cava is found in a semirigid space and bound by multiple lymph nodes. It has no valves, and about half of its surface is covered by pericardium.

The anatomic relations of the superior vena cava explain the frequency of the S.V.C. syndrome in carcinoma of the lung. Its close proximity to the right mainstem bronchus and lung, its proximity to multiple lymph nodes that drain the lung, its thin wall, its low intravascular pressure and its location in a semirigid compartment make it easy to understand this complication. The signs and symptoms that develop in these patients are the result of the venous hypertension produced by obstruction of the superior vena cava. The anatomic obstruction is usually slowly developing, and collateral vessels form to drain the upper part of chest, arms and head to the azygos through the intercostal veins. Acute total obstruction of the superior vena cava is uniformly lethal in animals. The tolerance of man to slow superior vena cava obstruction depends on the extent and rapidity of the occlusion, and on the adequacy of the collateral vessels that develop to decompress the upper chest, arms and head. Obstruction above the level of drainage of the azygos vein into the superior vena cava is better tolerated than is obstruction below the level of azygos drainage, because the collaterals formed in the former are more effective in decompressing the venous drainage from the upper part of the body.

The obstruction of the superior vena cava in man can be due to: 1) a large mass obstructing the superior vena cava by extrinsic compression; 2) a thin web or tumor mass compressing; 3) intravascular extension of tumor into

the superior vena cava. All of the above can be accompanied by intracaval thrombosis, which can be partial, or complete.

In 52 autopsied cases, it was found that 22 (44 percent) had complete occlusion of the S.V.C. after radiotherapy (7). Thrombotic occlusion of the superior vena cava probably explains the lack of response to radiotherapy of case No. 4 and No. 7, (Table I).

The full blown clinical picture of the superior vena cava syndrome presents with edema of the face, arms and upper torso. The patient often has cyanosis of the face and chest, with distended collateral veins. All this is often accompanied by shortness of breath.

Cerebral edema and petechial hemorrhages in the brain, which are due to increased intra-cranial pressure secondary to the venous hypertension, account for the cerebral symptoms. These symptoms may range from somnolence, to vertigo, to loss of consciousness, and may progress to seizures and coma. Death can be due to the cerebral picture, or to loss of respiratory center control, or to respiratory obstruction due to edema of the glottis or lower airways.

The syndrome should be suspected in any patient with edema of the face or arms and an abnormal chest X-ray. The usual chest X-ray abnormality is a mass in the right superior mediastinum. The latter, accompanied by the described clinical picture is pathognomonic of the superior vena cava syndrome. We do not feel that a superior vena cavogram is required for diagnosis of the syndrome. In fact, some authors state that access to veins of the upper thorax or arms is contraindicated (8). Radionuclide venography is effective, carries a low risk, and is preferred by some investigators for diagnosis and follow-up of superior vena cava obstruction. In idiopathic mediastinal fibrosis, the chest X-ray often shows no abnormality.

Histologic confirmation of the clinical suspicion of a malignant process should proceed forthwith since the patient may suffer a rapid demise before any therapy is started, as in case No. 8, Table I. It is accepted that if the superior vena cava syndrome causes severe symptoms, the patient can be treated with radiotherapy, or chemotherapy if a lymphoma is suspected, prior to the histologic confirmation.

The workup should include: Chest X-ray, PA and lateral, sputum cytology three daily samples, and fiberoptic bronchoscopy. If all are negative, and the patient can tolerate anesthesia, a limited thoracotomy should be done to obtain tissue for a diagnosis. We feel strongly that all of the above should be done within a few days of admission. There exists danger in extending the workup of this oncologic emergency to several weeks.

Management

Since the superior vena cava syndrome is a local problem, we recommend and use the least toxic local therapy to attempt relief of the S.V.C. obstruction. It is generally agreed that treatment for this oncologic emergency is radiotherapeutic. The field should include all gross tumor with a 2 cm margin, in addition to the hilar, mediastinal, and supraclavicular nodes. Therapy should be started by high dose fractionation, (400 rad daily for 3 days) and then reduced to 180-200 rad daily, five fractions per week. The total dose should be in the range of 3,000-5,000 rad, and it should be individualized according to the histology and the general condition of the patient. Green et al, (2), have shown that high fractionation early in therapy causes more rapid decompression without adding noticeable edema to the irradiated tissue. In Hodgkin's Disease, a common lymphoma

to present with the S. V. C. syndrome, the usual total dosage used is 4,000 rad in 4 weeks. The total dosage recommended for a bronchogenic carcinoma is 5,000 rad in 5 weeks. The spinal cord should not receive a dose in excess of 5,000 rad with 200 rad fractions, and less if the magnitude of the fractionations exceeds 200 rad. Much has been said about "Radiation Induced Edema" but Green, et al. (2) demonstrated the absence of inflammatory reaction and edema following radiotherapy.

The authors know of no controlled randomized prospective trial which shows that adding chemotherapy to the described radiotherapeutic regime improves the results. There is also no data to show that steroids, or anticoagulants combined with radiotherapy improve results. Nevertheless, some investigators have used chemotherapy exclusively in the management of this emergency, and claim that in lymphoma the results are comparable to those attained with radiotherapy. Others use a chemotherapy course to ameliorate the S. V. C. syndrome, and then attempt anesthesia with limited thoracotomy for biopsy. This is usually followed by radiotherapy.

Pérez, et al. (5) have reported that about 10-20 percent of patients live more than 24 months after the diagnosis. In our series of 8 patients (Table I); of 6 with carcinoma of the lung, two (33 percent) had significant palliation of symptoms. Case No. 2 lived 204 days, and case No. 6 was asymptomatic at last follow-up approximately 150 days after the diagnosis.

In a large series reported from Memorial Cancer Center in New York, reviewing their experience from 1926-1958, in 3,650 lung cancer patients, they found 137 cases (3.4 percent) with the superior vena cava syndrome (6). The median survival for this group

of 137 cases was 158 days.

Levitt, S. H., et al (9), found in a randomized trial of 28 patients that nitrogen mustard given at a dose of 0.4 mg/kgm body weight followed in 3-8 days by radiation did not improve the results obtained with radiotherapy alone; and in fact, the morbidity and mortality was worsened in the group receiving nitrogen mustard.

In an addition to the series reported in 1965 (6), Salsali & Cliffton reported in 1969 (7) that in 210 patients with the superior vena cava syndrome, the median survival of those treated with radiation with or without chemotherapy was about 8 months.

To summarize, the superior vena cava syndrome is a frequent oncologic emergency in our milieu, and although the entity has been well described for many years, it is often misdiagnosed and mismanaged. The goal of management is a rapid diagnostic workup, and palliative radiation therapy to alleviate symptoms. Even if patients are not cured, or their survival prolonged, we have shown that relief of obstruction and symptoms can improve the quality of life in some of these unfortunate patients. The best local therapy is radiotherapy.

We recommend that patients with edema of the face and/or arms and an abnormal

chest X-ray, be referred to an institution where a multimodal approach can be used in planning diagnosis and therapy. Surgeons, radiotherapists, and medical oncologists should participate in management decisions from the time of admission.

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AVISO DE INTERES

La Junta Editora, consciente de su responsabilidad de hacer que el "Boletín" cumpla a cabalidad con su cometido de divulgar conocimientos médicos, elevar las normas de educación médica y al propio tiempo de llenar las necesidades de todos los compañeros médicos, ha acordado establecer una nueva Sección que se conocerá como "Sección de Preguntas".

Bajo esta nueva Sección, todos los compañeros tendrán la oportunidad de enviarnos preguntas médicas de casos difíciles o casos clínicos para opinión experta. Estas preguntas, con sus respuestas, serán publicadas en esta nueva Sección.

Las preguntas deberán ser enviadas a:

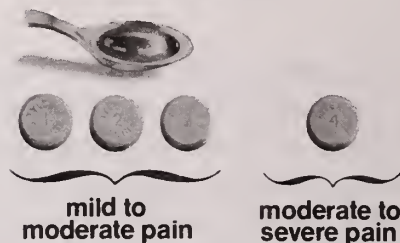
Boletín de la AMPR
Sección de Preguntas
Apartado 9387
Santurce, P. R. 00908

Esperamos sus preguntas.

Juan M. Aranda, MD
Presidente
Junta Editora

TYLENOL[®] with Codeine

tablets  / elixir 



Summary of Prescribing Information

Description

Tablets: Contain codeine phosphate[®]: No. 1—7.5 mg. ($\frac{1}{4}$ gr.); No. 2—15 mg. ($\frac{1}{2}$ gr.); No. 3—30 mg. ($\frac{1}{2}$ gr.); No. 4—60 mg. (1 gr.)—plus acetaminophen 300 mg.

Elixir: Each 5 ml. contains 12 mg. codeine phosphate[®] plus 120 mg. acetaminophen (alcohol 7%).

***Warning:** May be habit forming

Actions: Acetaminophen is an analgesic and antipyretic; codeine an analgesic and antitussive.

Contraindications: Hypersensitivity to acetaminophen or codeine.

Warnings: *Drug dependence:* Codeine can produce drug dependence of the morphine type and may be abused. Dependence and tolerance may develop upon repeated administration, prescribe and administer with same caution appropriate to other oral narcotics. Subject to the Federal Controlled Substances Act.

Usage in ambulatory patients: Caution patients that codeine may impair mental and/or physical abilities required for performance of potentially hazardous tasks such as driving a car or operating machinery.

Interaction with other CNS depressants: Patients receiving other narcotic analgesics, general anesthetics, phenothiazines, other tranquilizers, sedative-hypnotics or other CNS depressants (including alcohol) with this drug may exhibit additive CNS depression. When such a combination is contemplated, reduce the dose of one or both agents.

Usage in pregnancy: Safe use not established. Should not be used in pregnant women unless potential benefits outweigh possible hazards.

Pediatric use: Safe dosage of this combination has not been established in children below the age of three.

Precautions: *Head injury and increased intracranial pressure.* Respiratory depressant effects of narcotics and their capacity to elevate cerebrospinal fluid pressure may be markedly exaggerated in the presence of head injury, other intracranial lesions or a pre-existing increase in intracranial pressure. Narcotics produce adverse reactions which may obscure the clinical course of patients with head injuries.

Acute abdominal conditions. Codeine or other narcotics may obscure the diagnosis or clinical course of acute abdominal conditions.

Special risk patients: Administer with caution to certain patients such as the elderly or debilitated and those with severe impairment of hepatic or renal function, hypothyroidism, Addison's disease, and prostatic hypertrophy or urethral stricture.

Adverse Reactions: Most frequent: lightheadedness, dizziness, sedation, nausea and vomiting, more prominent in ambulatory than nonambulatory patients; some of these reactions may be alleviated if the patient lies down. Others: euphoria, dysphoria, constipation and pruritus.

Dosage and Administration: Dosage should be adjusted according to the severity of the pain and the response of the patient. It may occasionally be necessary to exceed the usual dosage recommended below in cases of more severe pain or in those patients who have become tolerant to the analgesic effect of narcotics. **TYLENOL with Codeine tablets** are given orally. The usual adult dose is: Tablets No. 1, No. 2, and No. 3: One or two tablets every four hours as required. Tablets No. 4: One tablet every four hours as required. **TYLENOL with Codeine elixir** is given orally. The usual doses are **Children (3 to 6 years):** 1 teaspoonful (5 ml.) 3 or 4 times daily; **(7 to 12 years):** 2 teaspoonful (10 ml.) 3 or 4 times daily; **(under 3 years):** safe dosage has not been established. **Adults:** 1 tablespoonful (15 ml.) every 4 hours as needed.

Drug Interactions: CNS depressant effect may be additive with that of other CNS depressants. See Warnings.

For information on symptoms/treatment of overdosage, see full prescribing information.

Full directions for use should be read before administering or prescribing.

TYLENOL with Codeine tablets are manufactured by McNeil Laboratories Co., Dorado, Puerto Rico 00646.

Caution: Federal law prohibits dispensing without prescription.

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McNeil Laboratories, McNEILAB, Inc.
Fort Washington, PA 19034

Sprains and Strains

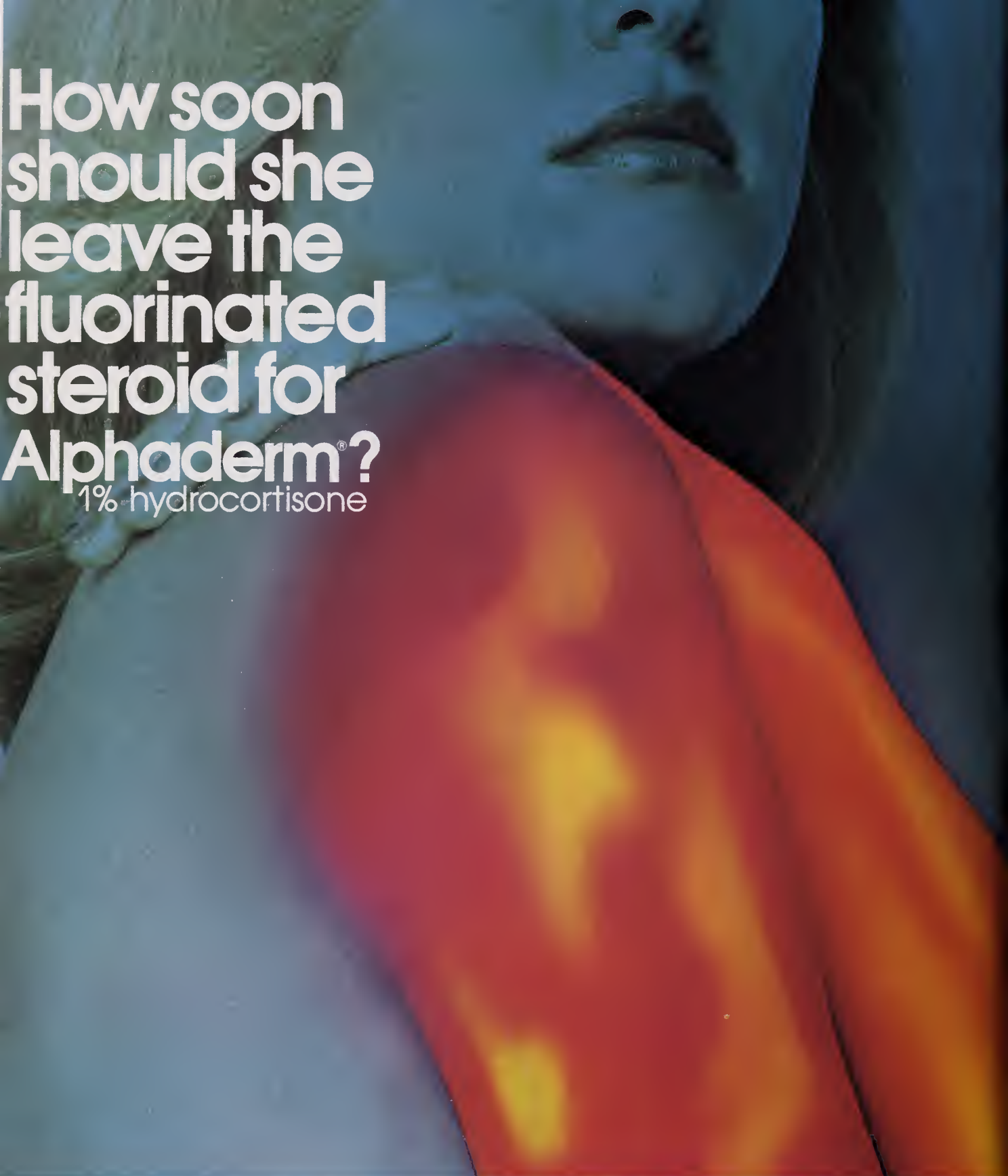
Potent pain relief without aspirin complications



TYLENOL[®]
with Codeine
tablets  / elixir 

Tablets Contain acetaminophen 300 mg plus codeine phosphate* as follows:
No. 1—7.5 mg (1/8 gr); No. 2—15 mg (1/4 gr); No. 3—30 mg (1/2 gr); No. 4—60 mg (1 gr)
Elixir Each 5 ml contains 12 mg codeine phosphate* plus 120 mg acetaminophen (Alcohol 7%)

*Warning: May be habit forming.



How soon should she leave the fluorinated steroid for Alphaderm®?

1% hydrocortisone

DESCRIPTION: Contains hydrocortisone 1% in a powder-in-cream base incorporating a hypermolar solution of urea 10% (carbamide), purified water, sorbitol, polyoxyethylene fatty glyceride, starch, white petrolatum, triglycerides of saturated fatty acids, isopropyl myristate, and sorbiton monolaurate. The near neutral pH of the formulation is made possible by the stabilized delivery system in which urea is absorbed by a polysaccharide powder matrix.

Alphaderm (1% hydrocortisone) Cream is hypoallergenic and contains no parabens or lanolin.

ACTION: Topical steroids are primarily effective because of their anti-inflammatory, anti-pruritic and vasoconstrictive actions.

INDICATIONS: For relief of the inflammatory manifestations of corticosteroid-responsive dermatoses.

CONTRAINDICATIONS: Topical steroids are contraindicated in those patients with a history of hypersensitivity to any of the components of the preparation.

PRECAUTIONS: If irritation develops, the product should be discontinued and appropriate therapy instituted.

In the presence of an infection, the use of an appropriate antifungal or antibacterial agent should be instituted. If a favorable response does not occur promptly, the corticosteroid should be discontinued until the infection has been adequately controlled.

The sooner the better.

It's the acute flare-up of eczema. Lesions are hot, raw, dry. You may need a potent fluorinated steroid to clear it up fast. But how long can you use the fluorinated steroids without increasing the risk of side effects such as atrophy, striae, telangiectasia?

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Add to that the known hydrating powers of 10% urea to keep skin moist, supple and smooth. Alphaderm® is an exquisite non-greasy cream that vanishes after a few seconds of gentle rubbing. Yet because it contains 26% petrolatum, it protects like an ointment. Alphaderm® is also ideal as initial therapy in delicate and intertriginous areas.

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If extensive areas are treated or if the occlusive technique is used, there will be increased systemic absorption of the corticosteroid and suitable precautions should be taken, particularly in children and infants.

Although topical steroids have not been reported to have an adverse effect on human pregnancy, the safety of their use in pregnant women has not absolutely been established. In laboratory animals, increases in incidence of fetal abnormalities have been associated with exposure of gestating females to topical corticosteroids, in some cases of rather low dosage levels. Therefore, drugs of this class should not be used extensively on pregnant patients, in large amounts, or for prolonged periods of time.

The product is not for ophthalmic use.

ADVERSE REACTIONS: The following local adverse reactions have been reported with topical corticosteroids, especially under occlusive dressings: Burning, Itching, Irritation, Dryness, Folliculitis, Hypertrichosis, Acneiform eruptions, Hypopigmentation, Perioral dermatitis, Allergic contact dermatitis, Maceration of the skin, Secondary infection, Skin atrophy, Striae, Miliaria.

DOSAGE AND ADMINISTRATION: Apply a small quantity of Alphaderm (1% hydrocortisone) Cream to affected areas twice daily.

HOW SUPPLIED: Alphaderm (1% hydrocortisone) Cream is available in:
NDC 0149-0705-12 tubes of 30 grams
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Tail of whipworm
(*Trichuris trichiura*)

Vermox[®]: the only anthelmintic highly effective against whipworm.

	Cure Rate	Egg Reduction
VERMOX [®]	68%*	93%**
Mintezol ¹	35%†	45%††
Antiminth ²	Not Indicated	
Povan ³	Not Indicated	

Also highly effective against roundworm and hookworm*

Since whipworm, roundworm and hookworm are all soil-borne helminths, mixed infections are not uncommon. Only one anthelmintic exhibits high efficacy rates for all three nematodes: whipworm—68%; roundworm—98%; hookworm—96%. That agent is VERMOX.[®]

Please see following page for Summary of Prescribing Information.

**Broad-spectrum coverage
in mixed helminthic infections**

Vermox[®] TABLETS
(mebendazole)



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*Committed to research...
because so much remains to be done.*

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JP1 023



**Broad-spectrum
coverage in mixed
helminthic infections**

TABLETS
Vermox[®]
(mebendazole)

Contraindications VERMOX is contraindicated in pregnant women (see: Pregnancy Precautions) and in persons who have shown hypersensitivity to the drug.

Precautions **PREGNANCY:** VERMOX has shown embryotoxic and teratogenic activity in pregnant rats at single oral doses as low as 10 mg/kg. Since VERMOX may have a risk of producing fetal damage if administered during pregnancy, it is contraindicated in pregnant women.

PEDIATRIC USE: The drug has not been extensively studied in children under two years; therefore, in the treatment of children under two years the relative benefit/risk should be considered.

Adverse Reactions Transient symptoms of abdominal pain and diarrhea have occurred in cases of massive infection and expulsion of worms.

Dosage and Administration The same dosage schedule applies to children and adults. The tablet may be chewed, swallowed or crushed and mixed with food. For the control of pinworm (enterobiasis), a single tablet is administered orally, one time.

For the control of roundworm (ascariasis), whipworm (trichuriasis), and hookworm infection, one tablet of VERMOX is administered, orally, morning and evening, on three consecutive days.

If the patient is not cured three weeks after treatment, a second course of treatment is advised. No special procedures, such as fasting or purging, are required.

* Mean cure rate of VERMOX[®] in treating whipworm; cure rate range of 61-75%. Data on file at Janssen Pharmaceutica Inc.

** Mean egg reduction of VERMOX[®] in treating whipworm; egg reduction range of 70-99%. Data on file at Janssen Pharmaceutica Inc.

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Health and Safety Tip

From the American Medical Association

535 North Dearborn Street/Chicago, Illinois 60610

Sun Tanning Harmful To Skin, Says AMA

Sun Tanning Harms Skin

What does your doctor think of sun tanning?

He's against it.

If you should ask your doctor whether there is any health value to sun tanning, he would have to answer "No." If you asked him whether sun tanning might hurt you, he would have to reply "Yes."

Sunning, overdone, can cause severe burn. Sunning, done modestly, can produce a golden tan that gives an illusion of health and well being. But that golden tan often leads to premature aging and wrinkling of the skin, to premature "age spots" on the hands and neck, and to skin cancer.

So, once again, the American Medical Association advises Americans everywhere against suntanning.

But, your doctor also is well aware that millions of Americans will ignore this advice this summer. They will flock to the swimming pools and beaches through the warm months to bask in the sun. They will stretch out on the grass in the back yard, or on the roof terrace, or in the nearest park.

If you insist on getting a tan this summer despite medical advice to the contrary,

here's how to do it without burning.

On the first day of sunning, allow 15 minutes on each side. The second day 20 minutes. The third day 25 to 30 minutes. By the third day the skin should begin to brown. Thereafter proceed at the best pace for your own skin to tan without burning. At the first sign of redness, get out of the sun.

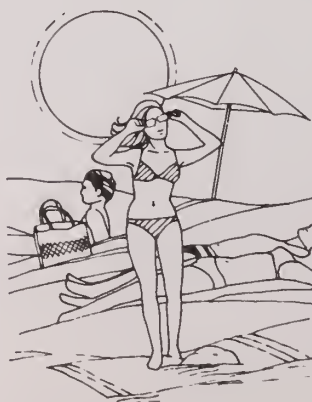
It isn't easy to confine sun time to only half an hour on the first day at the vacation resort. But you can't stretch it very much. If you try to double the exposure time to hurry the tan, you'll burn. And then return from vacation with a peeling skin instead of a tan.

Time of exposure also should be adjusted to time of day. The sun's rays are hottest between 10 a.m. and 2 p.m. After 5 p.m. you aren't likely to burn much.

There are creams and lotions that screen some of the rays and reduce danger of burning. But if the cream should screen all rays, there would be no tanning. You can still burn through creams if you stay out long enough. Also, water in the pool or perspiration washes away much of the cream in a short time.

Tanning removes most of the natural oils from the surface of the skin and many sunbathers find it helpful to use a cream or oil to relieve dryness.

Enjoy the outdoor life of the summer months. Don't overdo the suntanning.



June, 1980
Frank Chappell
Science News Editor
AMA

NOCARDIOSIS PULMONAR

PRESENTACION DE UN CASO Y REPASO DE LA LITERATURA

Rafael Quiñones, MD, Guillermo J. Vázquez, MD y
Carlos H. Ramírez Ronda, MD

Las infecciones causadas por *Nocardia* asteroides son poco frecuentes. En los Estados Unidos se reconocen menos de 1,000 casos nuevos anualmente (1). A continuación presentamos un caso de nocardiosis pulmonar, en el que claramente se demuestra la presentación clínica no específica de esta enfermedad y se señalan las dificultades en el manejo y seguimiento de estos pacientes.

Presentación del Caso

Un hombre de 56 años de edad fue admitido al Hospital Universitario en diciembre de 1978 con un historial de pérdida progresiva de peso de alrededor de 30 libras, fiebres nocturnas, dolor en el hemitorax izquierdo y dificultad respiratoria por un período de aproximadamente 4 meses de duración. El paciente no reportó historial previo de hemoptisis, contacto con tuberculosis, infecciones pulmonares, o de fumar cigarrillos.

De la Sección de Enfermedades Infecciosas, Hospital Universitario. Programa de Entrenamiento en Enfermedades Infecciosas de la Escuela de Medicina-Universidad de Puerto Rico y Hospitales Afiliados y Departamento de Medicina Escuela de Medicina, San Juan, Puerto Rico.

Favor de pedir reimpresos a: Guillermo J. Vázquez, MD, Jefe Sección Infectología, Hospital Universitario, Depto. de Medicina, Recinto Ciencias Médicas, Sección Enfermedades Infecciosas, GPO Box 5067, San Juan, Puerto Rico 00936.

A la exploración física se observó un paciente que lucía crónicamente enfermo, desnutrido y con una temperatura oral de 37.8°C. Los hallazgos pertinentes se limitaban al examen de los campos pulmonares donde se encontró la ausencia de sonidos respiratorios y matidez a la percusión en el hemitorax izquierdo. El resto del examen físico era esencialmente normal.

El hemograma obtenido inicialmente demostró una hemoglobina de 13.2 gm por ciento; 6,500 leucocitos, 77 por ciento de los cuales eran segmentados, 22 por ciento linfocitos y 1 por ciento eosinófilos. La radiografía del torax mostró opacificación de las dos terceras partes inferiores del pulmón izquierdo compatible con un derrame pleural. El resto de los exámenes de laboratorio no señalan anormalidad alguna.

El diagnóstico preliminar fue el de cáncer pulmonar. Ese mismo día se le practicó una toracentesis que reveló la presencia de un exudado con 2,000 células blancas por ml., 85 por ciento monocitos y 15 por ciento segmentados. Cultivos y tinciones del esputo para bacterias, hongos y organismos ácido-resistentes fueron negativos. La prueba de tuberculina demostró un área de induración de 20 mm a las 48 horas. Al quinto día de su admisión se le practicó una biopsia pleural la cual se interpretó como compatible con un proceso inflamatorio no específico.

El paciente continuó con fiebre moderada y fue comenzado el 19 de diciembre en penicilina, dos millones de unidades administradas por vía endovenosa cada cuatro horas. El 22 de diciembre se le practicó una broncoscopia la cual reveló un des-

plazamiento en la carina hacia el lado derecho y estenosis del bronquio principal izquierdo. El día 27 de diciembre se decidió discontinuar la penicilina y comenzar un curso empírico con isoniazida y etambutol. Estas drogas fueron también discontinuadas el día 8 de enero, al observarse que el paciente no mejoraba y que la función hepática comenzaba a deteriorarse. Se propuso repetir la biopsia pleural y poner un tubo de pecho para drenaje pero el paciente abandonó el hospital sin autorización médica el día 9 de enero de 1979.

El 13 de enero de 1979, regresó al hospital aquejando dolor severo en el hemitorax izquierdo y dificultad respiratoria marcada. En esta ocasión se insertó un tubo de pecho que drenó 1,700 ml. de un líquido purulento el cual fue cultivado. Debido a que tenía fiebre y leucocitosis se comenzó en penicilina y gentamicina. El 30 de enero (53 días después de su primera admisión), se aísla *Nocardia asteroides* en tres cultivos del líquido pleural. Los antibióticos antes mencionados se discontinuaron y se le comenzó en sulfisoxazole (Gantrisin ®) 3 gramos por vía oral cada 4 horas. Durante la admisión se le hizo un cintiograma cerebral que fue reportado como normal. El paciente mejoró con este tratamiento y fue dado de alta el 29 de marzo, en sulfisoxazole y con drenaje continuo del pulmón izquierdo.

En septiembre de 1979, el paciente fue hospitalizado nuevamente con dolor en el hemitorax izquierdo y abundante secreción purulenta a través del tubo de pecho. Se encontró muy deteriorado, estuporoso, con moderada rigidez nuchal y dolor difuso en el abdomen. El conteo de leucocitos fue de 17,300 con 78 por ciento segmentados y 22 por ciento linfocitos. Todos los demás laboratorios y cultivos fueron normales o no ocurrió crecimiento. Se le practicó una punción lumbar la cual demostró un líquido cefalorraquídeo cristalino con 31 células blancas, 150 mg de proteínas y una concentración de glucosa entre los límites normales. Las tinciones de tinta china y de Ziehl Neelsen fueron negativas. Se le hizo un electroencefalograma, una tomografía cerebral computarizada y un cintiograma de hígado y bazo, que fueron negativos. En vista de su pobre estado se decidió añadir ampicilina 2 gm. IV cada 6 horas al tra-

tamiento, pero no se observó ninguna mejoría. Se repitió la punción lumbar que reveló persistencia de proteínas elevadas siendo normales los otros parámetros. Se optó por discontinuar el sulfisoxazole y empezar un tratamiento con ampicilina, eritromicina 500 mg. cada 6 horas por vía oral y trimetoprim-sulfametoxazole (TMP-SMX, Bactrim ® Septra ®) 6 tabletas cada seis horas. Luego de unos días de iniciada esta nueva modalidad de tratamiento el paciente comenzó a mejorar. Su temperatura se normalizó y también su estado de conciencia. Después de 14 días en este tratamiento se discontinuó la eritromicina.

En la placa de pecho no hubo cambios marcados. Se le repitió la tomografía computarizada cerebral la cual no demostró cambios significativos. Se dio de alta en TMP-SMX para ser seguido en las clínicas de enfermedades infecciosas.

Discusión

La nocarditis fue descrita por Eppinger en el 1890. Es una infección supurativa poco común, que afecta principalmente al pulmón, pero con marcada tendencia a invadir el cerebro y otros órganos. Puede presentarse de forma aguda, aunque es más común que curse en forma crónica tal como sucedió con nuestro paciente.

La distribución de *Nocardia* es mundial y su ambiente natural es el terreno. Es una bacteria aeróbica que forma hifas ramificadas por lo cual erróneamente se agrupaba entre los hongos. Tiñe gram-positivo y es ácido resistente cuando se utiliza la tinción de Ziehl Neelsen modificada. Filamentos ramificados gram-positivos en un extendido sugieren nocardiosis o actinomicosis. Esta última puede distinguirse de *Nocardia* porque es anaerobia, por su configuración en granos de azufre y porque no tiñe con Ziehl Neelsen modificado.

La bacteria llega al hombre a través de la vía aérea o por la contaminación de heridas.

No existe la transmisión de hombre a hombre. Es una enfermedad que afecta fundamentalmente a personas de edad avanzada, a pacientes inmunocomprometidos, individuos con cáncer, transplantados, diabéticos y a quienes padecen de proteinosis alveolar (4, 2). Nuestro paciente carecía de enfermedades como éstas y quizás fue una razón para no pensar inicialmente en este diagnóstico. Cabe recordar que se han reportado casos donde el hallazgo de una infección como ésta es la primera manifestación de un paciente con una malignidad subyacente (7, 9).

Patológicamente puede presentarse como un absceso pulmonar. La histología es la de un granuloma supurativo a base de polimorfonucleares, linfocitos y células plasmáticas (2). Otras formas patológicas son: el nódulo solitario, fibrosis progresiva o neumonía necrotizante. En el cerebro, puede causar abscesos múltiples o inflamación purulenta de las meninges. También puede invadir órganos vecinos como el corazón, hígado, bazo y riñón.

Un 70 por ciento de los casos de nocardiosis se presentan como enfermedad pulmonar, con fiebre, sudoración nocturna, pérdida de peso, anorexia, tos, esputos purulentos, dysnea y dolor de pecho (7). Estos síntomas son similares a los hallados en la tuberculosis pulmonar, hecho que de no tenerse en cuenta pueden distraer nuestra atención hacia esta otra entidad. Nuestro paciente, con una prueba de tuberculina positiva, llegó a incluso a recibir dos semanas de tratamiento antituberculoso sin ésta haberse demostrado.

La radiografía de pecho puede revelar diferentes hallazgos: nódulos solitarios, nódulos múltiples, neumonía cavitaria de paredes gruesas, bronconeumonía y empiema pleural (2). Nuestro paciente se presentó con una empiema de difícil manejo. Al igual que con muchos otros pacientes de nocardiosis el diagnóstico inicial fue el de una malignidad del pulmón.

Sin lugar a dudas los hallazgos clínicos apuntaban hacia ese diagnóstico.

En un 20 a 30 por ciento de los casos hay afectación del sistema nervioso central y puede incluso ser la primera manifestación de la enfermedad (3). La clínica es la de un absceso cerebral o meningitis purulenta. Nuestro paciente se mostró estuporoso con rigidez de nuca en su última hospitalización. Pensando en que el paciente hubiese desarrollado esta complicación se le hizo una punción lumbar y otras pruebas no invasivas. Las manifestaciones neurológicas desaparecieron luego de instituirse un tratamiento adecuado.

La única manera de diagnosticar nocardiosis es teniéndola en mente y sabiendo que todo paciente, principalmente el inmunocomprometido, con enfermedad pulmonar, cerebral o cutánea, puede estar sufriendo esta condición. Este diagnóstico ha de hacerse aislando la bacteria. El material ideal para el diagnóstico bacteriológico es el tejido obtenido por medio de biopsia, aunque el esputo, el lavado bronquial, el fluído pleural y el pus de otras lesiones deben siempre teñirse y cultivarse. Debemos de tener en mente que nocardia no es un oportunista común de las vías respiratorias superiores, ni tampoco es un contaminante habitual del laboratorio (2). Por ello en todo paciente en el cual se aise *Nocardia* en esputo, debe de considerarse un hallazgo importante y amerita una confirmación. El organismo crece con facilidad en los medios usuales de cultivo de hongos, como Sabouraud y la infusión corazón-cerebro, además de crecer en los medios para el cultivo de tuberculosis como el de Lowenstein Jensen (7). El crecimiento en medio aeróbico lo diferencia de actinomicetes responsables de cuadros clínicos parecidos. Todo cultivo debe mantenerse en medios de cultivos por lo menos dos semanas. La bacteria suele crecer en menos tiempo, pero puede tardar

dando origen a falsos negativos. Las pruebas serológicas no son de utilidad para el diagnóstico.

A menudo el paciente de nocardiosis se complica y es común la tendencia a fistulizar, siendo sorprendente como desde el pulmón la bacteria se abre camino a intestino, hígado, piel y otros órganos. Esto a veces obliga hacer otros estudios complementarios cuando se evalúan estos pacientes. Nuestro paciente desarrolló náuseas, vómitos y dolor abdominal en un momento dado. Tuvimos duda de si se trataba de extensión de la infección hacia el aparato digestivo, un proceso neoplástico gastrointestinal o el efecto de los medicamentos administrados. Estudios radiográficos excluyeron las dos primeras posibilidades.

Las sulfonamidas han reducido la mortalidad de un 100 por ciento a un 25-40 por ciento (1). Este panorama ha mejorado aún más con el uso combinado de sulfonamidas, ampicilina y eritromicina (5). También se han reportado, últimamente, buenos resultados con el uso de TMP-SMX en aquellos casos que no responden a tratamiento convencional. En nuestro paciente no se observó una respuesta adecuada a sulfisoxazole ni a la combinación de ésta con ampicilina y eritromicina, no obstante, al añadir TMP-SMX hubo un cambio dramático en todos los aspectos clínicos. La persistencia de imágenes radiográficas anormales, en nuestro caso, pueden muy bien ser explicadas por la cronicidad del proceso infeccioso.

Es sumamente importante el hecho de que para obtener curación todo tratamiento debe mantenerse por lo menos durante un año (3, 7). Esto implica que el médico ha de saber ganarse la confianza del paciente y debe mantener en éste un estado de optimismo y positividad. Nuestro paciente rehusó nuestra cooperación en dos ocasiones. Quizás algunas

circunstancias de nuestro medio hospitalario no permitieron que ningún médico lograra establecer una buena comunicación con nuestro paciente y que esto conllevara a rehusar el tratamiento durante su primera admisión. Esto es tal vez la más temida complicación no solo de nocardiosis sino de muchas otras entidades clínicas.

Conclusión

Nocardia es una enfermedad poco común en nuestros hospitales. Tal vez su incidencia es mayor de lo que sospechamos. Su morbilidad y mortalidad son elevadas. Sin embargo el diagnóstico y tratamiento temprano aseguran un relativo buen índice de curación.

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Please see last page for brief summary, including warnings, precautions, and adverse reactions.

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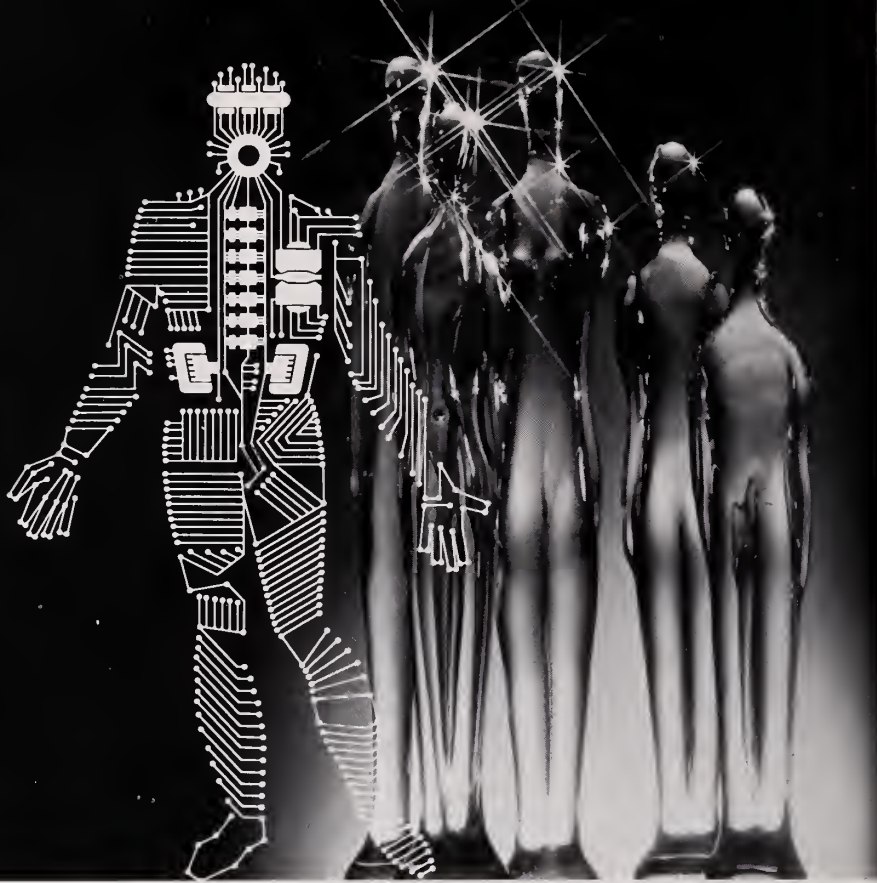




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En este número del Boletín se publican las ponencias de los participantes de un panel que se llevó a efecto durante la última convención anual de la Asociación Médica de Puerto Rico y que se tituló "Lengua y Medicina".

Esta actividad representa un hecho histórico para nuestra Asociación pues, hasta donde yo sé, por lo menos en los tiempos modernos, este tema nunca había sido abordado, ni siquiera presentado, formalmente dentro del marco de nuestro programa científico anual. No sólo tiene significado histórico este panel. Su importancia también estriba en haber podido alertar a los miembros de nuestra profesión sobre el deterioro, cada vez mayor, que se ha hecho evidente en el uso del idioma por nuestros médicos.

La realización de este panel se inició con una propuesta del Dr. Salvador Arana Soto. El Dr. Arana había sido designado por el Ateneo Puertorriqueño para organizarlo como parte de una serie de "coloquios" que dicha institución, con la ayuda de la Fundación Puertorriqueña de las Humanidades, programó para el año 1979. Como el Dr. Arana conocía mis preocupaciones por el uso impreciso y erróneo, a veces alarmante, de nuestra lengua en el campo de la medicina, me pidió que me hiciera cargo de la encomienda. No necesitó el prestigioso galeno insistir mucho para que yo aceptara organizar y presidir dicho panel. Se necesitaba ventilar abiertamente el problema y esta ocasión se prestaba para ello. Al aceptar yo la invitación, la Asociación Médica se convirtió en el tercer auspiciador.

No sólo se trata de criticar el "Spanglish" de aquí, o el "Neoricanismo" de allá, o el "Inglañol" sobre el cual ha escrito nuestro Salvador Tió. Se trata también de señalar otros factores más profundos, más fundamentales, que han sido responsables de un deterioro en la educación del hombre, deterioro que diariamente estamos viendo, leyendo y oyendo en el transcurso de nuestras consultas. Tampoco se trata de eliminar un idioma o de sustituir uno con otro. Se trata de uno expresarse correctamente en los dos. Todo esto es discutido por los ponentes.

Se determinó que la manera más práctica de abordar el tema es la de presentarse desde tres puntos de vista: 1) El Problema Como Existe Actualmente; 2) Las Raíces del Problema; y 3) El Remedio al Problema. Se tuvo la suerte de conseguir tres médicos cuyas serias inclinaciones hacia el campo literario y lingüístico son bien conocidas. Los Doctores José Ramírez Rivera, Rodrigo Menéndez Corrada y Manuel E. Paniagua aceptaron desarrollar el tema bajo los anteriores títulos y en el orden que han sido anotados. Así se publican.

Repito, son tres ponencias de valor lingüístico, literario, e histórico en el campo de nuestra medicina. Lector, no dejes que pasen inadvertidas.

José M. Torres-Gómez, MD

LENGUA Y MEDICINA

Rodrigo Menéndez Corrada, MD

La lengua y la medicina siempre han estado íntimamente relacionadas; así la exigencia más común que le hacemos a un paciente cuando lo examinamos es ¡Saque la lengua! Pero esta vez, como lo han hecho saber bien claro los participantes del coloquio que me han precedido, se trata de la lengua de los médicos, no la de los pacientes. En términos generales han señalado que existen serias deficiencias en la forma que la clase médica del país maneja esa lengua.

Creo que debemos puntualizar desde el principio que el lenguaje que usamos comúnmente los médicos en Puerto Rico es el mismo del resto de los puertorriqueños y que como tal tiene las mismas características, adolece de los mismos defectos y ostenta las mismas virtudes del habla actual de nuestro país. Sobre este español apenas pienso ocuparme que bastante han dicho sobre el particular los filólogos y lingüistas estudiosos en la materia y por tanto mucho mejor capacitados que yo para pasar juicios. No puedo, sin embargo resistir la tentación de confesar que me inclino de parte de los que creen que el español de Puerto Rico no es ni peor ni mejor que el que habla el resto de los hispanohablantes. El haber estado 80 años bajo la influencia norteamericana no ha hecho mella en nuestro idioma vernáculo hasta el punto de comprometer nuestra mutua comprensión con Latinoamérica o España. Las diferencias entre el español de Puerto Rico y el de Argentina, por ejemplo, no son mayores de las que existen entre los respectivos idiomas de México y Argentina digamos. Es más, parece que con el

enorme auge de la comunicación entre países en nuestros tiempos el signo actual es el universalismo, no la fragmentación del idioma, y así me lucen proféticas las palabras de Menéndez-Pidal cuando dice: “La pronunciación de un idioma se formará mañana con acento universal. La palabra radiodifundida pesará sobre el habla de cada región, las variedades dialectales se extinguirán por completo.”

Pero aunque no acierte totalmente el pronóstico de Menéndez-Pidal y subsistan diferencias, estas no tendrán importancia si no entorpecen la comprensión y repetimos con el Arcipreste de Hita: “non hay mala palabra si es bien entendida”. De modo que en cuanto al uso del vernáculo en los quehaceres ordinarios del médico no veo ningún problema especial.

Otra cosa es, sin embargo, el uso del idioma como vehículo de la comunicación hablada o escrita con propósitos científicos o literarios entre profesionales o en círculos cultos o en la docencia. Aquí hay exigencias legítimas que van más allá de la mera comprensión. Aquí tradicionalmente hay imperativos de corrección, estilo, precisión, elegancia, amenidad y hasta uso imaginativo del idioma. No basta con que nos entiendan hay que decirlo bien dicho.

¿Y hasta qué punto estamos cumpliendo esa norma los médicos? ¿Estamos justificados los médicos en creernos una clase culta? Debíamos suponer que sí.... Después de todo son ocho años de escuela elemental, cuatro años de escuela superior, cuatro años de bachi-

llerato o su equivalente, más cuatro años de estudios de medicina propiamente más por lo regular dos o tres años más de estudios postgraduados los que hay detrás de cada médico. Cerca de 20 años de estudios formales o formativos que debían dar al cabo de ellos por lo menos un ciudadano bien pulido; "hombre acabado", como diría Papini. Lamentablemente no parece ser así a juzgar por lo que han dicho los deponentes que me han precedido y yo estoy de acuerdo de que posiblemente buena parte de los médicos de Puerto Rico no saben expresarse culta o correctamente en inglés o en español o en ningún idioma.

Al examinar este problema para identificar las raíces de su origen lo primero que se nos ocurre es: pues habrá fallado lo único que puede haber fallado, nuestro sistema educativo con sus normas, con su currículo, con sus métodos de enseñanza, con sus maestros. Pero cabe preguntarse ¿acaso la necesidad perentoria de nuestra sociedad es de médicos cultos o de médicos competentes? Sobre este particular tengo pocas dudas; estamos produciendo médicos competentes para el ejercicio de la medicina. El problema es que también queremos que sean cultos y no parece que esto sea una exigencia descabellada dado el tiempo y el dinero que se está gastando en prepararlos. Al decir que sean cultos no solamente pretendemos que hablen y escriban bien, también queremos que se interesen en la investigación, que inventen, que descubran, que hagan labor creativa científica o literaria o social. Si ésta es nuestra meta creo que nos conviene escudriñar cuidadosamente el currículo pre-médico.

¿Qué debemos hacer para despertar la curiosidad — que si no es madre — es por lo menos abuela de la invención? El tema es amplísimo y naturalmente es motivo de preo-

cupación, no solo entre nosotros, sino en otros países. La educación médica se discute constantemente en la prensa norteamericana y no es asunto concluido en ningún sitio.

El segundo tema que se me ocurre se refiere más exclusivamente al problema del idioma. ¿Hasta qué punto el descuidado hablar de nuestros médicos jóvenes es signo de nuestros tiempos? Se habla mal, como se viste mal. El rechazo de todo lo formal, lo ortodoxo, lo convencional. La glorificación del desaliño, de la vagancia, que se inició con la revolución, o tal vez aberración, hippie que aunque mitigada aún se deja sentir. Se desprecia la gramática como se desprecia la corbata o el chaquetón. Esta actitud ante la vida, esta postura, debían haberla superado nuestros jóvenes cuando llegan a médicos pero en los que persiste no siempre es signo de inmadurez y, quizás huelga señalarlo, no está reñida con una dedicación genuína y sorprendente a los enfermos. Es más, estos médicos barbudos y desaliñados son a menudo muy idealistas y muy competentes.

Y por último como posible factor operante en el deterioro palpable en el uso del vernáculo en nuestros médicos señalamos la convivencia de dos idiomas en Puerto Rico y especialmente en la medicina de Puerto Rico. El español; el cuarto idioma del mundo en cuanto al número de sus hablantes y vehículo de una cultura recia, aquí más que en otros sitios, dado a nuestros nexos especiales con los Estados Unidos, está sufriendo los embates del segundo lenguaje más hablado en el mundo y el lenguaje actual de la ciencia y el progreso mundial; la lingua franca de la medicina: el inglés. La pujanza intelectual de los angloparlantes es apabullante no hay más que repasar la lista de los Premios Nobel— ahora mismo acaba de adjudicársele el codiciado premio a un antillano como nosotros,

un antillano de la raza negra pero que habla inglés. Esa hegemonía del inglés inunda de anglicismos no solo el idioma de Puerto Rico sino el de todas las naciones del orbe incluyendo la Francia, tan celosa de su idioma, España, Rusia, Japón, etc.

El médico que quiere estar al día en su medicina en Puerto Rico o quizás en cualquier parte del mundo no tiene más que leer lo que aparece en la literatura médica norteamericana, con eso basta y sobra y quizás no vale la pena leer nada más. El médico investigador que quiere publicar el fruto de sus esfuerzos y someterlo al juicio de sus pares ha logrado su objetivo si consigue publicarlo en la prensa médica norteamericana. Si leer en inglés, si publicar en inglés es lo que dictan las circunstancias actuales, ¿cómo vamos a detener la influencia del inglés? Y así comparto la opinión de Rubén del Rosario cuando escribe: "Pero mientras subsistan las rela-

ciones políticas y culturales con el mundo anglamericano, mientras sean ellos que inventen cosas nuevas y nosotros los que las recibamos, mientras los pueblos hispánicos prefieran la retórica a la creación científica, tendremos anglicismos, progresivamente más anglicismos".

Las relaciones con el mundo anglosajón pueden muy bien seguir. Tengo, sin embargo, la sospecha que no en balde el Destino nos ha puesto en la encrucijada de dos culturas. El Destino nos ha lanzado un guante situándonos ante ruedo tan amplio, tendremos que ser muy aptos para desempeñarnos airoosamente, los tiempos requieren talento, esfuerzo, flexibilidad, ánimo. Pensemos como Nietzsche: "Lo que no logra destruirme, me hace más fuerte." Y recordemos el caso del pueblo judío a quienes sus vicisitudes milenarias lo han depurado convirtiéndolo en lo que De Gaulle caracterizó como: "Un pueblo elite".

CONTESTACIONES A PULMONARY QUIZ

1. B

2. E

3. E

4. A

5. D

6. C

7. B

8. C

9. D

10. C

LA PROFESION Y EL MAL USO DEL IDIOMA ESPAÑOL

José Ramírez Rivera, MD

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Centro Médico de Mayaguez

Introducción

No se nos pide analizar el uso de la lengua en una profesión o actividad cualquiera o de comentar sobre el estilo que usamos para narrar acontecimientos de mayor o menor importancia en la vida humana; se nos solicita que observemos perceptiblemente el uso de nuestro idioma en la práctica de la medicina, en el importante quehacer de proteger la vida misma.

Empezaremos destacando que el español no es un dialecto de limitado alcance. Es un lenguaje cuyo vigor y rigurosa efectividad estaba ya de manifiesto desde la época colonizadora. Los orígenes de la lengua literaria española anteceden con mucho al descubrimiento de América, pero es precisamente en el 1492, el año cuando se produce este magno acontecimiento en la historia del hombre, que se publica la primera gramática española, la del maestro Nebrija. Desde ese momento el desarrollo lingüístico en la Península Ibérica y en Hispanoamérica han sido paralelos y complementarios. Mientras España asimilaba vocablos acuñados en otros países

de Europa — en Francia, Italia, Alemania, Portugal — Hispanoamérica enriquecía el lenguaje con vocablos amerindios autóctonos. Por esta vía Puerto Rico y las Antillas menores hicieron también su aportación: *Güicharo* y *maraca*, nombres de instrumentos musicales, y *yuca* y *maíz*, menciones de vegetales totalmente desconocidos hasta entonces por el europeo, son excelentes ejemplos de los centenares de voces aportadas a la lengua española por las antillas.

En esta reunión no habremos de censurar la influencia taína en nuestra lengua; tampoco causarán desasosiego los galicismos que se popularizaron en España durante los siglos XVIII al XIX, ni los anglicismos que desde el XIX amplifican y prestan vigor al idioma.

Hoy queremos hacer hincapié en otra fase del tema: Nuestra dejadez intelectual ante el impacto nocivo del inglés en el lenguaje de la medicina en Puerto Rico. Señalaremos de paso otras facetas de nuestra limitación lingüística.

Observaciones y Comentarios

Existe en nuestro pueblo una marcada insensibilidad respecto a diversos vocablos y construcciones sintácticas del inglés que, al no ser debidamente adaptadas a nuestro idioma, le quitan lustre y claridad a la

Charla que formó parte del panel "Lengua y Medicina" auspiciado por la Asociación Médica de Puerto Rico, el Ateneo Puertorriqueño y la Fundación Puertorriqueña de las Humanidades, San Juan, Puerto Rico - Noviembre 7, 1979.

expresión hispánica; son usos léxicos y fraseológicos más bien torpes que inhiben el desarrollo de nuestra efectividad comunicativa y Profesional. Escuchar estos traslados incoherentes es particularmente penoso en los círculos médicos. Angustia oír la mezcla innecesaria y constante del español y el inglés en nuestras aulas y hospitales.

Es sorprendente que la mala adaptación de locuciones inglesas a nuestro idioma sea más intensa ahora que antes de la década del cuarenta, cuando un por ciento mayor de nuestros médicos se educaba en los Estados Unidos. Estos médicos regresaban al país conscientes de que se estaban trasladando a otra cultura; venían dispuestos a emplear los conocimientos adquiridos con arreglo a nuestra lengua y dentro del marco ambiental isleño. Por otra parte, los egresados recientes de las escuelas de medicina no parecen darse plena cuenta de las limitaciones que representa el expresarse en el lenguaje híbrido que corrientemente usan. El intenso contacto que han tenido en sus años formativos con el prestigioso desarrollo moderno de la técnica y la ciencia norteamericana los ha convencido, como está convenciendo a muchas otras personas en el Tercer Mundo, que lo norteamericano es lo efectivo y lo digno de imitarse, y comportándose de acuerdo con tales conceptos hablan al modo del norteamericano, aunque ello signifique *hibridizar* la lengua propia.

Salta a la vista en la presentación de historiales clínicos la pobreza del vocabulario y la falta de recursos de expresión sintáctica en español y en inglés de nuestros médicos. Y las limitaciones con nuestro idioma no son exclusivas de aquellos que han cursado sus estudios en la Isla, en Norteamérica o en otros países de la Cuenca del Caribe. Encontramos también profesionales que después de pasar seis o más años de estudios de medicina en

ambientes madrileños y salmantinos aún no saben expresarse con efectividad y soltura en español.

Además, al visitar las salas de hospitales, oímos a algunos médicos residentes dirigirse a pacientes recién conocidos de una manera descuidada y poco respetuosa, usando apelativos como "viejita, abuela y mijita". Estos tratamientos de indudables raíces populacheras proyectan una falsa intimidación vulgarizante, atentatoria contra la debida dignidad profesional, y contra la efectividad terapéutica que surge de una respetuosa relación médico-paciente. Un error aún más fundamental es encontrar corrientemente en nuestras experiencias postgraduadas médicos que se dejan seducir fácilmente por la sencillez de las expresiones anecdóticas que oyen de labios de sus pacientes cuando éstos intentan explicarles sus dolencias, o quienes, en su afán por reducir lo complejo a la simplicidad que se acostumbra en el medioambiente, aceptan como conceptos válidos interpretaciones erróneas del texto leído; hablamos de médicos cuya capacidad perceptiva y cuya efectividad terapéutica se ve lamentablemente entorpecida por una escasa y primitiva comprensión del idioma materno.

No es apropiado que envolvamos en el fabuloso ropaje del lenguaje lírico nuestros historiales o nuestras notas de evolución clínica; pero sí debemos exigir en tales documentos precisión de pensamiento y capacidad de exposición que se ajusten, con la dramática autenticidad que les corresponde, al nivel de la tragedia humana que analizamos. La falta de destreza para percibir y valorizar las variadas tonalidades de lo escuchado y de describir con fidelidad diferenciante lo observado, limita el diagnóstico a lo más conocido y reduce la medicina a un ejercicio de ensayos terapéuticos con frecuencia abocados al fracaso.

Quizás la invitación a figurar en este panel haya surgido del estudio que publicamos el Dr. Braulio Quintero y este servidor en el *Boletín de la Asociación Médica de Puerto Rico*, en julio de 1977 (1). En este trabajo recopilamos 97 términos de la lengua inglesa escuchados en las aulas y salas de medicina en el Centro Médico de Mayagüez, entre mayo de 1975 y abril de 1976. Seleccionamos solamente aquellas frases y palabras repetidas cinco o más veces por cinco personas diferentes. Excluimos otros anglicismos de uso común en español.

¿Por qué decir "chest pain" en vez de *dolor de pecho*, "blood sugar" por *azúcar sanguínea*, "GTT" por *prueba de tolerancia de glucosa*, o "ketoacidosis" por *cetoacidosis*? ¿Es "chronic brain syndrome" más claro que *síndrome cerebral crónico*? No apreciamos la ventaja de hacernos incomprensibles para nuestros hermanos de Hispanoamérica al extraer "blood gases" por *gases arteriales* y oír "wheezes" por *sibilancias*. Ni vemos la razón para sustituir "upper G. I. series" por *estudio del tracto gastrointestinal superior*, o "progress notes" por *notas de evolución*; como tampoco se justifican los usos de los otros ochenta y tantos vocablos de igual índole anglicista que pudimos oír y recoger durante el período citado.

Un mejor conocimiento de los dos idiomas que usamos, y una ortografía más correcta, mejorarían el cuidado que damos a nuestros pacientes. El empleo de frases lúcidas y universalmente comprensibles resulta de un pensar lógico y ordenado, y este pensar debe transcribirse en forma de órdenes médicas y observaciones clínicas claras y legibles. Los más ingeniosos y costosos métodos de diagnóstico y los más dramáticos avances terapéuticos se tornan peligrosos cuando se ordenan y describen en un lenguaje ambiguo.

Recientemente oímos a un distinguido radiólogo decir: - Si miramos esta radiogra-

fía, este "chest plate". Expresiones como ésta nos desconciertan, pues se repite en inglés lo dicho en español, como si se diera por sentado que el anglicismo posee *per se* el don natural de transmitir la idea con mayor claridad. El mundo de habla hispana fuera de Puerto Rico interpreta nuestra barbarie lingüística, a veces, como esnobismo, otras veces como lo que realmente es: una ignorancia injustificable de nuestra lengua materna.

Traducimos literalmente del inglés al español, por ejemplo: "history of" como *historia de* en lugar de *historial de*; reemplazamos continuamente la voz española: por *enema de bario* decimos "barium enema". Para colmo de males, pronunciamos mal muchas veces las dicciones inglesas: *escul siris* por "skull series". Por último, utilizamos frases torpes que son en realidad híbridos lingüísticos. He podido escuchar cosas como las siguientes: - Mira, Ramón, te mando un paciente con "G.I. bleeding" para un "rule out" de várices esofágicas. ¿No nos entenderíamos mejor, señores, si expresáramos esa sencilla solicitud sin la aparatosa mezcla de dos idiomas? Por ejemplo: - Mira, Ramón, te envío un paciente con sangrado gastrointestinal para excluir várices esofágicas.

No pretendemos que se modifique en todos sus detalles el arraigado sublenguaje que usamos. Es preciso reconocer que ciertos términos que en un principio el purista registra como signos de mal uso, terminan por ser parte de la expresión profesional por sus insustituibles dotes de brevedad, concisión y aceptación universal. Sirvan *shock* y *stress* como dos ejemplos excelentes de lo que acabamos de decir. Pero creemos, por otro lado, que las numerosas incrustaciones del inglés que hacemos a diario en nuestro vernáculo exceden la natural capacidad del idioma para la absorción de vocablos foráneos. Identifiquemos el inadecuado dominio del español que evidencian nuestros médicos por lo que es - una

desnaturalización de la lengua, signo de decadencia lingüística vernácula.

En los ámbitos de educación médica en el país no hemos notado todavía esta identificación. No se están corrigiendo activamente los hábitos de hondo arraigo en cuanto al mal uso del idioma, ni se está alentando el refinamiento de nuestras capacidades expresivas a los fines de lograr comunicarnos más efectivamente. No parece haber una actitud responsable y cuidadosa en cuanto a los usos respectivos del inglés y el español para poder llegar a dominar ambos idiomas, actitud que nos ayudaría enormemente a ampliar nuestro bagaje cultural y nuestra efectividad profesional.

Conclusiones

En los círculos médicos de Puerto Rico hemos desarrollado una Babel lingüística absurda, ridícula y ofuscatoria. El peligroso sublenguaje sólo se comprende a medias en el mismo grupo profesional que lo utiliza. Este grupo no ha aceptado la obligada responsabilidad de aprender a seleccionar los vocablos

que enriquecen la lengua y de saber descartar los rasgos léxicos que la denigran y la adulteran. Tendremos que decir con Don Pedro Salinas, en su ensayo *Aprecio y Defensa del Lenguaje* (2), que nuestro medio profesional médico considera la lengua como un regalo que se le hizo al nacer y no como un prodigioso instrumento para expresar su ser con exactitud y finura.

La lengua, dice T. Navarro Tomás, no tiene otro destino que aquél a donde la conducen las gentes que de ella se sirven. Esperamos que el médico puertorriqueño no haya adoptado una postura pasiva permanente frente a su lenguaje materno y esté dispuesto a hacer suyo todo lo que quieran echarle encima los ignorantes. La descolorida jerga entre dos lenguas que empleamos es inoperante tanto en Hispanoamérica como en los países de habla inglesa. Hay que rechazarla.

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CONTESTACIONES A ACUTE MYOCARDIAL INFARCTION QUIZ

1. False
2. False
3. False
4. False
5. False
6. True
7. False
8. False

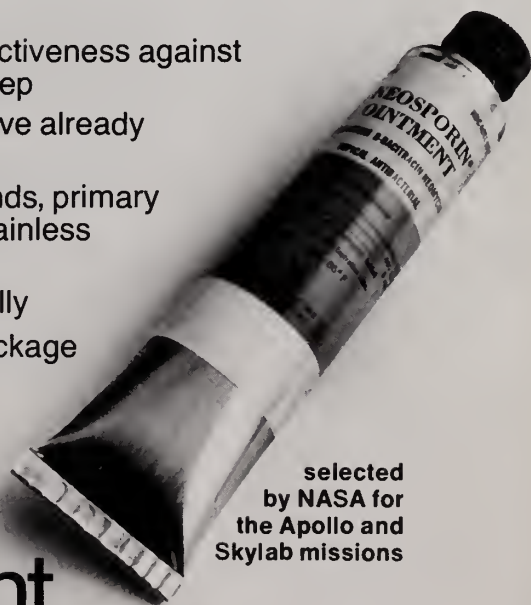
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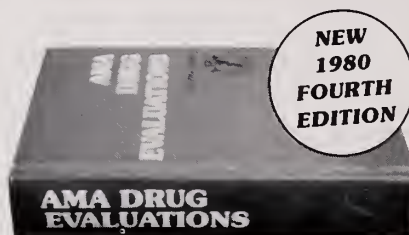
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PONENCIA SOBRE LENGUA Y MEDICINA “EL REMEDIO AL PROBLEMA”

Manuel E. Paniagua, MD

El organizador de este acto ha seguido el esquema que usamos los médicos en la discusión de las distintas entidades nosológicas. Así, el doctor Ramírez nos ha presentado el cuadro clínico discutiendo muy acertadamente los síntomas, signos y otras manifestaciones de la dolencia lingüística que padecemos. Luego, el Dr. Menéndez Corrada ha hurgado en la etiología multifactorial del problema y su patogenia y patofisiología. Se me ha asignado a mí la difícil tarea de buscarle tratamiento.

Siguiendo el paralelo con el enfoque médico, deseo recordarles que, desde el punto de vista de objetivo a alcanzarse, el tratamiento de cualquier enfermedad puede ser específico, sintomático o paliativo. Llamamos tratamiento específico a aquel que va dirigido a eliminar o contrarrestar la o las causas que lo origina (cuando éstas se conocen — por lo que es imperativo hacer primero un diagnóstico correcto); sintomático es aquel que va dirigido a aliviar los síntomas en lo que se descubre una causa, hace efecto el tratamiento específico o recupera espontáneamente; paliativo es realmente una variante del tratamiento sintomático que va dirigido a hacer sentirse mejor al incurable y ayudarle a bien morir.

Como dije anteriormente, ya el doctor Ramírez nos hizo una magnífica descripción del enfermo y su dolencia. Nada tengo que añadir a esto pero, para aquellos de ustedes que están interesados, he traído unas copias del glosario preparado por nosotros en el De-

partamento de Medicina del Hospital Municipal de San Juan principalmente para uso de nuestros residentes, en un esfuerzo por ayudar a resolver el problema según detallaré más adelante.

Sobre las tres causas principales que mencionó el Dr. Menéndez Corrada en su análisis, también tengo muy poco que añadir y voy a discutir o, más bien, a mencionar las posibles e improbables soluciones.

El relajamiento de la disciplina en general y de la disciplina intelectual en particular, es algo que ya forma parte de la evolución social de nuestra cultura occidental. El problema ha sido analizado por sociólogos, psicólogos y filósofos sin que se haya llegado a un acuerdo sobre sus consecuencias y ni siquiera si es posible modificarlo aunque fuera deseable o conveniente. Nada podemos ofrecer como tratamiento específico aquí.

El segundo factor etiológico, el conocido deterioro en la calidad de la instrucción pública y privada merece un poco más de atención. El sistema educativo de un país es resultado de la filosofía educativa de ese país, la cual, a su vez, refleja su filosofía de vida y su sentido de valores. El sistema educativo de Puerto Rico es copia infiel e inexacta del sistema de los Estados Unidos. Lo de infiel e inexacta se refiere al hecho de que se ha calcado sin tratar de adaptarlo a las realidades puertorriqueñas; al contrario, como un nuevo Procrusto, se ha tratado de forzar al puertorriqueño para que encaje en el modelo calcado. Pero, aún dejando ésto a un lado,

el sistema educativo norteamericano deja mucho que desear desde el punto de vista filosófico-intelectual, ya que siendo reflejo del sentido de valores de dicho país, más su evolución histórica, demuestra un mayor énfasis en la importancia de los resultados obtenidos que en la forma de obtenerlos. En el plano del lenguaje, esta actitud ha resultado en una falta de conocimiento de su propia lengua inglesa que llega frecuentemente hasta la falta de respeto aún entre personas de nivel universitario.

Además, hay una tendencia de la filosofía pedagógica "moderna" (por lo menos en Estados Unidos y, naturalmente, también aquí) de tratar de hacer el proceso de aprendizaje no sólo interesante si no también más fácil mediante el uso y el abuso de las llamadas ayudas audiovisuales, uso de calculadoras, etc. Yo creo que el proceso de aprendizaje, aunque debe ser agradable e interesante, conlleva necesariamente un esfuerzo, de parte del educando (no hay ni debe haber incompatibilidad entre esos dos conceptos). Ese afán de facilitar el aprendizaje propende a la vagancia intelectual, a buscar el camino más fácil, a no hacer el esfuerzo necesario para ser más claros y más correctos en nuestra exposición oral.

¿Qué remedio podemos ofrecer contra esto? Lo único práctico que se me ocurre es lo que estamos haciendo un pequeño grupo de médicos interesados en el problema que estamos llevando a cabo una campaña personal y dando el ejemplo a nuestras colegas más jóvenes, especialmente aquellos que están adiestrándose en nuestras instituciones, mientras

están bajo nuestra influencia.

En cuanto a la tercera causa que menciona el Dr. Menéndez Corrada, la hegemonía del inglés como lengua médica universal, no creo que tenga, o que deba tener tanta importancia como causal del problema que nos ocupa. En primer lugar, el limitarse a la literatura médica norteamericana es una forma de coloniaje intelectual, pues hay mucho de valor en la literatura médica de otros países. Por otro lado, también en la literatura médica norteamericana se publica bazofia científica. Y, en cuanto al idioma, las versiones al inglés de trabajos originales japoneses, italianos, etc., no son superiores a los expedientes clínicos escritos por muchos de nuestros colegas. No hay duda que un médico que quiera estar al día en los conocimientos debe saber inglés, por lo menos lo suficiente para leerlo y comprenderlo, pero para poder dominar una lengua extraña hay que conocer primero la propia y usarla correctamente.

El tratamiento dirigido a esta última causa sería lógicamente un refuerzo de la enseñanza del inglés *previa* enseñanza y dominio del vernáculo lo que implicaría una mayor eficiencia técnica de nuestro sistema educativo y una mejor orientación filosófica y pedagógica, cosas que creo muy difíciles de conseguir en las circunstancias actuales.

En resumen, después de haber oído el planteamiento del problema y el análisis de las posibles causas me siento muy pesimista en cuanto a su posible solución y solamente puedo ofrecer algunos paliativos.

MYCOSIS FUNGOIDES

Miguel Vázquez Botet, MD and Jorge L. Sánchez, MD

A 58-year-old female was seen at the clinic because of persistent pruritic skin lesions of several years duration which in the last few months had increased in size and number. She denied other symptomatology or past history of systemic disease.

The physical examination was negative except for shotty inguinal lymphadenopathies and the cutaneous findings. Two types of skin lesions were present, mainly in the trunk and the extremities; one of them consisted of round and circinate orange-pink patches with little or no alteration on their surfaces and the other of erythematous scaly infiltrated plaques some showing central clearing (Fig. 1).

1. The most appropriate clinical diagnosis is:

- a) Psoriasis
- b) Contact Dermatitis
- c) Leukemia Cutis
- d) Mycosis Fungoides
- e) Neurodermatitis

Two skin biopsy specimens were ob-



Figure 1

tained. The one from a patch showed perivascular infiltrates of mononuclear cells in the upper dermis with small discrete collections within the epidermis without microvesiculation and no striking nuclear atypia (Fig. 2). The

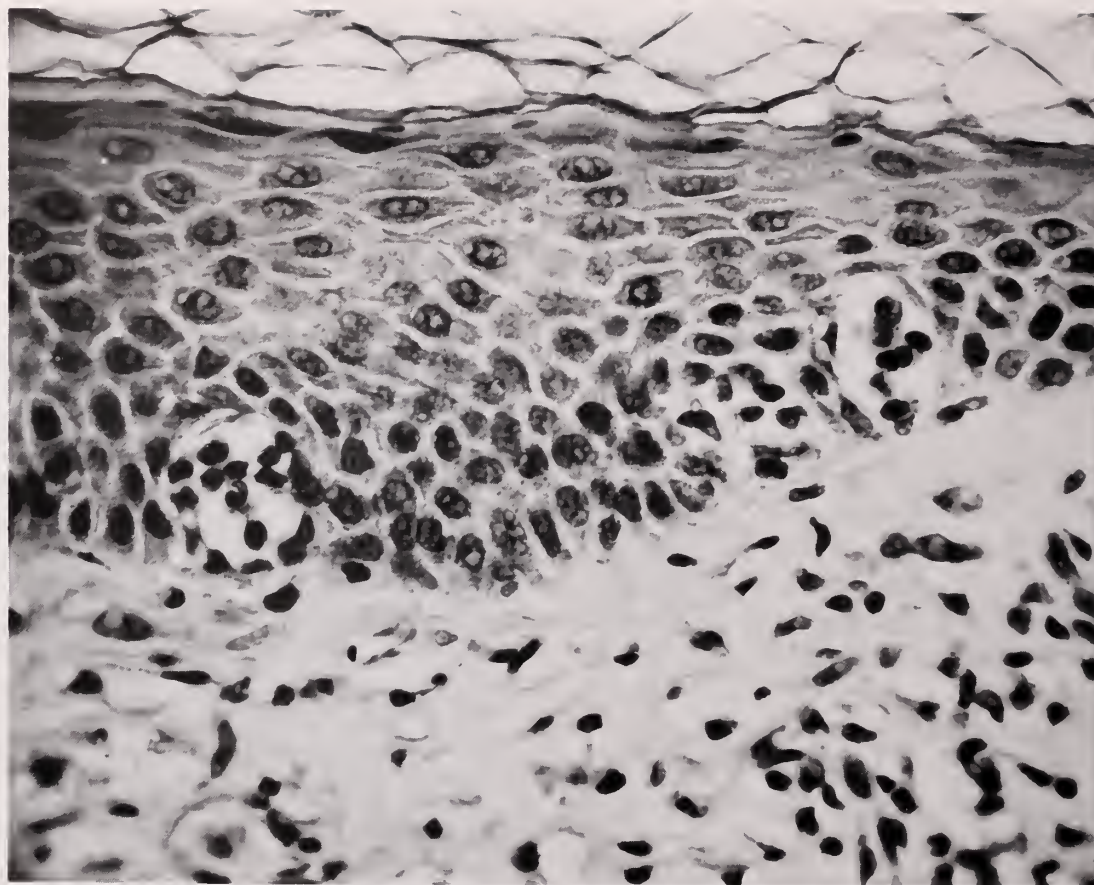


Figure 2

specimen from a plaque showed a lichenoid bandlike infiltrate of mononuclear cells that extends across the upper part of the dermis parallel to the epidermis partially obscuring the dermoepidermal interface (Fig. 3). There were large numbers of mononuclear cells within the epidermis which were atypical (large, hyperchromatic and pleomorphic) and larger than the mononuclear cells in the dermis.

The histologic findings were reported by the dermatopathologist as diagnostic of mycosis fungoides:

2. At this stage, you should recommend the patient to:

- a) Start topical corticosteroid therapy
- b) Start on systemic chemotherapy
- c) Do A and B only after bone marrow aspiration
- d) Admit to hospital for staging procedures

She was admitted to the hospital and extensive laboratory studies were performed including CBC, U/A, SMAC₂₀, Chest X-Rays, Skeletal Survey, EKG, bone marrow aspiration,

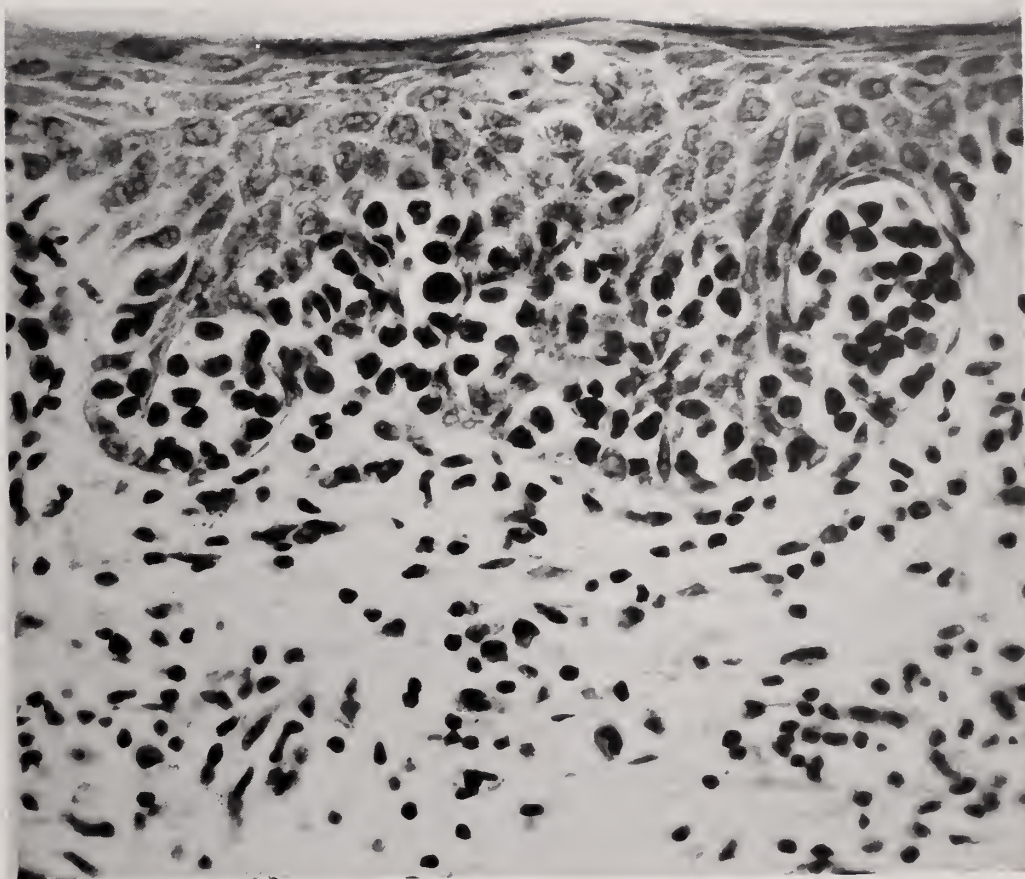


Figure 3

liver and spleen scan and inguinal lymph node biopsy. All were negative for lymph node, visceral and bone marrow extracutaneous disease. Consequently, the stage of her disease was determined as Mycosis Fungoides, stage 'II' (skin involvement consisting of plaques).

3. Accepted treatment modalities for this stage of disease are:

- a) Topical nitrogen mustard
- b) Total body surface electron beam therapy
- c) Oral psoralens with long-wave ultraviolet light (PUVA)

d) Topical 1, 3-bis (2-chloroethyl)-1 nitrosourea (BCNU)

Comments

Mycosis fungoides (MF) is a T-cell lymphoma usually seen between the ages of 45 and 70 whose initial manifestations are in the skin. Early in the disease, the appearance of the lesions may mimic those of other benign dermatosis like psoriasis, contact dermatitis, neurodermatitis and other eczematous processes. The cutaneous lesions may include patches, papules, plaques and tumors; the latter are commonly associated with a poor prognosis and internal

involvement. As the disease progresses, generalized symmetrical lymphadenopathy occurs followed later by visceral involvement. The Sésary syndrome is generally regarded as the leukemic variant of MF, although this opinion is not shared by all.

Staging procedures should be performed in every case for the evaluation of extension of the disease. The staging system is as follows:

STAGE DESCRIPTION

I	Erythematous plaque or generalized erythema.
II	Indurated plaque or exfoliative erythroderma or both.
III	Tumors with or without papules, plaques, or generalized erythroderma.
IV	Histologically confirmed lymph node involvement.
V	Visceral involvement.
a)	without a leukemic phase
b)	with a leukemic phase

The most widely used forms of treatment for stage I and II are topical nitrogen mustard (mechlorethamine, HN_2), total body surface electron beam therapy, topical 1, 3-bis (2-chloroethyl) -1 nitrosourea (BCNU), and oral psoralens with long-wave ultraviolet light (PUVA).

Systemic chemotherapy is indicated in patients with advanced plaque or tumor

stage MF not manageable by topical therapy or radiation and in the presence of lymph node, visceral, or bone marrow involvement (stages III, IV, V). A number of drugs are used singly and in combination in the treatment of systemic MF, including methotrexate, mechlorethamine, cyclophosphamide, doxorubicin, vinca alkaloids, bleomycin, azaribine, prednisone and BCNU. Despite the use of such agents, the prognosis for survival of patients with systemic MF for more than a year or two is poor.

Correct answers:

- 1) D
- 2) D
- 3) A, B, C, D

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P U L M O N A R Y Q U I Z

1. Chronic bronchitis is often accompanied by hypoxemia. The cause of this observed hypoxemia is:
 - A. hypoventilation
 - B. ventilation/perfusion abnormalities
 - C. right to left shunting
 - D. decreased chemoreceptor responsiveness to oxygen
2. Patients with early mild chronic bronchitis usually will show significant alterations to flow in very small airways (less than 2mm in diameter) with little or no alterations to flow in larger airways. At this stage of disease, which of the following would most likely be abnormal?
 - A. F_{ev}
 - B. total airway resistance
 - C. maximum mid expiratory flow rate
 - D. peak expiratory flow
 - E. frequency dependence of compliance
3. Which of the following agents would not be appropriate to start during an acute asthmatic episode?
 - A. epinephrine
 - B. terbutaline
 - C. methyl prednisolone
 - D. aminophylline
 - E. cromolyn sodium
4. Which of the following will increase intracellular concentration of cyclic AMP by stimulating adenocyclase production?

- A. epinephrine
 - B. aminophylline
 - C. propranolol
 - D. cromolyn sodium
5. All of the following have been associated with extrinsic allergic alveolitis except:
- A. working with moldyhay
 - B. mushroom work
 - C. pigeon breeding
 - D. cleaning farm silos
 - E. cork work
6. The reason combined drug therapy is used in tuberculosis is:
- A. to allow for lower dosages of individual drugs thus preventing toxic drug effects
 - B. major synergistic effects between common antituberculous drugs
 - C. to prevent the development of drug resistance
 - D. historical reasons that are probably no longer valid
7. Only 50 percent of patients with pneumococcal bacteremia and pneumonia have pneumococcus grown from their sputum cultures. Possible explanations for this discrepancy include all of the followings except:
- A. Institution of antibiotic therapy before sputum is collected
 - B. certain strains are facultative anaerobes and need CO₂ to grow on surface solid media
 - C. sensitivity to optochin
 - D. oral secretions instead of purulent sputum are collected for cultures

- E. confusion with streptococcus viridans by inexperienced laboratory personnel
8. A therapeutic theophylline level is the following:
- A. 5-10 ugms/ml
 - B. 30-40 ugms/ml
 - C. 10-20 ugms/ml
 - D. 20-30 ugms/ml
9. The most common sign of ethambutol toxicity is:
- A. loss of yellow visual discrimination
 - B. loss of red visual discrimination
 - C. loss of orange visual discrimination
 - D. loss of green visual discrimination
10. Which of the following is the most frequent complication of staphylococcal pneumonia?
- A. brain abscess
 - B. acute endocarditis
 - C. pneumothorax
 - D. kidney abscess

(Contestaciones en página 181)

M E D I Q U I Z

HEMODYNAMICALLY UNSTABLE PATIENT WITH ACUTE MYOCARDIAL INFARCTION

The principal cause of death in acute myocardial infarction (AMI) continues to be cardiogenic shock. The diagnosis of cardiogenic shock is the clinical diagnosis of peripheral hypoperfusion (brain, kidney, skin). Disturbances in heart rhythm, circulating volume and mechanical properties of the heart (valves, pericardium, right ventricular distensibility and wall integrity) can produce reversible cardiogenic shock. Extensive muscle damage with loss of muscle power will produce cardiogenic shock (when more than 40 percent of left ventricular muscle is rendered inactive). Vasodilators, inotropic agents and mechanical assistance devices will help most of these patients but long term survival is determined by the amount of remaining viable myocardium.

TRUE OR FALSE

1. The severity of left ventricular dysfunction in acute myocardial infarction is independent of prior myocardial infarctions.
2. Mechanical problems rarely affect left ventricular performance in patients dying of cardiogenic shock during acute myocardial infarction.
3. All patients in cardiogenic shock will benefit from digitalization.
4. There is little prognostic correlation in large clinical subgroups of patients with acute myocardial infarction between hemodynamic measurements and clinical classification.
5. Interventricular septum rupture is always a lethal complication of myocardial infarction.
6. Papillary muscle rupture is seen more often in inferior than in anterior myocardial infarction.
7. Rupture of the heart is rarely seen in patients suffering their first myocardial infarction.
8. Cardiogenic shock can only be recognized by complex, invasive hemodynamic measurements.

Guillermo Cintrón, MD
Director
Coronary Care Unit, VAH

(Contestaciones en página 185)

VALOR Y SEGURIDAD DE LA CATETERIZACION CARDIACA DURANTE ENDOCARDITIS INFECTIVA ACTIVA

Albert E. Raizner, MD, Houston Texas - Am J. Card. Dec./79, Vol. 44 p. 1306-1310

Se revisaron 35 casos de pacientes previamente sometidos a cateterismo (CAT): 30 de ellos por fallo cardíaco severo y 5 por sepsis persistente o embolización recurrente en consideración a intervención quirúrgica. El promedio de días desde la admisión al hospital hasta el cateterismo fue de 19 días (1-60 días). El diagnóstico pre-cateterización había sido incompleto o incorrecto en 23 de 35 pacientes. El cat. demostró lesiones múltiples valvulares en 7 pacientes en los cuales no se habían sospechado y documentó envolvimiento valvular único en 6 pacientes con soplos que hacían pensar en lesiones múltiples valvulares por endocarditis. En 6 pacientes se encontraron abscesos del anillo valvular y en todos se confirmó operatoriamente. En 3 casos se encontró un "shunt" de izquierda a derecha asociado a infección de un seno de valvula roto. Todos los 35 casos fueron confirmados de endocarditis infecciosa tanto por cultivos de sangre y ecocardiografía, sumado al cuadro clínico como por confirmación patológica en el momento de operación o posterior autopsia. *Staphylococcus aureus* fue el organismo causal más frecuente (51 por ciento). Habían 7 mujeres y 28 hombres y las edades fluctuaron de 20-77 años (Prom = 38 años).

La única complicación fue una fibrilación atrial transitoria en un solo caso. Ninguno tuvo embolia, infarto o deterioro hemodinámico post-cateterismo.

Conclusión: El cateterismo pre-operatorio provee de gran información anatómica y hemodinámica al cirujano permitiéndole un juicio lógico a la hora de tomar una decisión de índole quirúrgica. Operar sin tener un cateterismo puede ser no exitoso o fatal si el diagnóstico ha sido incompleto. Se recomienda por lo tanto cat. cardíaco en todo paciente con endocarditis en que se contemple cirugía.

(Sometido por J. R. Couto MD, VAH)

REHABILITATION PRINCIPLES IN THE CARE OF GYNECOLOGIC AND OBSTETRIC PATIENTS

B. J. Maly, Archives of Physical Medicine and Rehabilitation, 61: 78-81, 1980.

Hay muy poca literatura que tome en consideración la rehabilitación en problemas gineco-obstétricos. La autora considera la salud de tejidos del piso de la pelvis como los más importantes dentro del grupo músculo esquelético, produciendo entre otros incontinencia urinaria, dispareunia, prolapso de órganos pélvicos, etc. Kegel, en trabajos anteriores ha establecido que la mayor parte de la problemática reside en el músculo pubococcígeo y desarrolló el uso de un "perineómetro" con el cual hizo determinaciones sobre la fuerza contractil mínima necesaria para evitar incontinencia.

La rehabilitación de pacientes gineco-obstétricos se limita actualmente a diversos ejercicios enseñados en programas educativos sobre el parto, los cuales aparentemente son inadecuados por su corta duración y la ausencia de seguimiento post parto.

Se diseñó el estudio actual para determinar la aplicabilidad de principios de rehabilitación comparando las variables de ejercicio versus no ejercicio. El estudio incluyó 136 mujeres en las cuales se encuentra una incidencia menor de incontinencia urinaria en las mujeres que se ejercitaron. Otras modalidades de entrenamiento y tratamiento, tales como electro-estimulación y educación muscular dirigidas por miembros del equipo de rehabilitación pueden ser importantes en el futuro como prevención y tratamiento en la paciente gineco-obstétrica.

(Sometido por Frank W. López, MD)

PAIN IN PATIENTS WITH SPINAL CORD INJURY

Cecil Cepomuceno, MD, Philip R. Fine, PhD, J. Scott Richards, PhD, Hilda Gowens, CA, Samuel L. Storer, MD, Ubop Rantanuabol, MD, Roger Houston, PA, Arch Phys Med Rehab. 60: 605-609, Dec. 79.

Para este estudio de dolor continuo después de una lesión al cordón espinal, se desarrolló un cuestionario y se envió a 356 pacientes de trauma medular que habían sido hospitalizados, 200 (56 por ciento) de los cuales devolvieron el cuestionario completamente lleno. De éstos, se refirieron al malestar como una sensación anormal 160 (80 por ciento) y 96 (48 por ciento) se refirieron como dolorosa. Las sensaciones anormales fueron por primera vez sentidas 6 meses después del trauma por 105 pacientes, de 7 meses a 4 años después del trauma por 39 y de 4 años en adelante después del trauma o que no sabían el tiempo en 16 pacientes. La localización del dolor variaba y no correlacionaba con el nivel de la lesión. En 30 por ciento de los que reportaban sensaciones anormales, la localización del dolor permaneció estacionaria, mientras que en 17 por ciento cambió con el tiempo. La intensidad del dolor se describía de severa a extrema por 25 por ciento; 44 por ciento indicaron que interfería con actividades del diario vivir. Un aumento del dolor con el tiempo fue notado por 41 por ciento. No se consideró como circunstancias agravantes actividad, inactividad, cambios del tiempo y el sobre esfuerzo. El descanso y la medicación fueron citados como factores que aliviaban. Aproximadamente 38 por ciento de los que experimentaban dolor usaban medicinas pero solo 22 por ciento obtenían alivio consistente de su uso. Los pacientes de lesiones bajas estaban más dispuestos a canjear una hipotética oportunidad de recuperación y/o pérdida de funciones fisiológicas readquiridas como alivio para el dolor que pacientes de lesiones altas.

(Sometido por Rafael Seín, MD, VAH)

EL SINDROME DE INSERCIÓN DEL SEMIMEMBRANOSO: CAUSA FRECUENTE Y TRATABLE DE DOLOR CONTINUO DE LA RODILLA

Hans I. Weiser, MD, Arch. Phys Med. Rehabil. 60: 317-319, 1979.

La inserción del semimembranoso causa dolor en el aspecto medial de la rodilla. Este dolor se agrava con el ejercicio, bajar escaleras y al doblar la rodilla. En todos los pacientes se encontró; dolorimiento en la parte distal del músculo semimembranoso; la rotación pasiva de la rodilla producía dolor en la parte medial y la presión digital en el área de inserción del tendón del semimembranoso producía un dolor exquisito. Cien pacientes con síndrome de inserción del semimembranoso con el padecimiento entre 1 a 12 meses, o más, fueron tratados con inyección local de lidocaína y triamcinolome. Todos experimentaron alivio inmediato del dolor. Se consiguió alivio a largo plazo de los síntomas y signos en 58 pacientes, 30 de los cuales requirieron repetición de la inyección entre 3 a 5 meses.

El dolor y discapacidad disminuyó en otros 9 pacientes. Hubo 18 tratamientos en que no se consiguió la mejoría. La mayoría de los pacientes eran mujeres con exceso de trabajo de casa, sobretodo antes de días festivos.

(Sometido por Rafael Seín, MD, VAH)

GOLD-INDUCED CHANGES IN THE MORPHOLOGY AND FUNCTIONAL CAPABILITIES OF HUMAN MONOCYTES

Ugai, K. U., Ziff, M., and Lipsky, P. E. - Arthritis and Rheumatism 22 (12), 1352-60, Dec. 1979.

The capacity of gold compounds to induce mor-

phologic changes and alterations in the functional activity of human mononuclear phagocytes in vitro was examined. Human peripheral blood mononuclear cells were incubated with gold sodium thiomalate (25 ug/ml) for 96 hours. As a result, mononuclear phagocytes developed electron dense precipitates within phagolysosomes, as well as marked dilatation of these organelles. Gold incubation also altered a number of mononuclear phagocytes functions. While viability and adherence were unaffected, the capacity to spread on surfaces was diminished. Pinocytosis of soluble proteins and phagocytosis of opsonized sheep erythrocytes were impaired, but Fc mediated particle binding was not. These data indicate that gold can alter certain functional activities of mononuclear phagocytes and support the idea that the major action of gold in rheumatoid arthritis results from its capacity to alter mononuclear phagocytes function.

(Submitted by Edwin Mejías, MD, VAH)

GASTRIC CANCER DETECTION IN GASTRIC ULCER DISEASE

Mountford, R. A., Brown, P., Salmon, P. R., Alwarenga, C., Neumann, C.S., and Read, A. E. *Gut* 21: 9-17, 1980.

Los autores presentan un estudio retrospectivo de todos los pacientes con úlcera gástrica que se diagnosticaron o evaluaron en su unidad endoscópica en un período de tres años. El tiempo promedio de seguimiento fue de dos años. De un total de 265 casos 37 (14 por ciento) tenían úlceras malignas. El grupo de pacientes con úlcera maligna presentaron más frecuentemente con pérdida de peso, anorexia, náusea, vómitos y multiplicidad de síntomas. Con la excepción de ulceración en el fondo del estómago que se asoció con malignidad, ni la localización de la úlcera ni la coexistencia de inflamación péptica en el duodeno ayudaron a definir la naturaleza de la úlcera. Estudios radiológicos fueron altamente ineficaz en diferenciar ulceración benigna de maligna. La inter-

pretación endoscópica fue más certera. En conjunto con biopsias y citología tomadas durante las endoscopías se diagnosticaron tres casos de cáncer gástrico superficial. (Hay varios reportes de 90 por ciento de sobrevivencia a los cinco años después de cirugía cuando se opera cáncer gástrico superficial). Los autores abogan porque se estudien endoscópicamente todos los casos de úlcera gástrica.

(Sometido por Angel Olazábal, MD)

EXPOSICION A LAS RADIACIONES EN EL CATETERISMO CARDIACO

Martínez de Ubago, J. L., Colman Dejean, T., Figueroa Olavarría, A., et al. *Rev. Esp. Cardiol.* 32 (5): 457, 1979.

Para la eficacia óptima de un laboratorio de hemodinámica se precisa la especialización del personal médico y un alto número de exploraciones por año. Representando estos cateterismos una fuente considerable de radiación.

En un período de 14 semanas se realizaron 284 cateterismos con control dosimétrico de radiación a nivel de los ojos, manos, y gónadas, utilizando dos sistemas radiológicos diferentes. Se encontró que hay mayor cantidad de radiación dispersa en los sistemas radiológicos con tubos sobre la mesa, y que la fluoroscopia es responsable de más de 90 por ciento de la radiación. Los resultados demuestran que la exposición en las manos es relativamente baja no importa el sistema utilizado y que en las gónadas es insignificante. Las dosis recibidas por el cristalino fueron considerablemente altas, siendo tres veces mayor con el tubo de rayos X sobre la mesa.

Se concluye que debe reducirse el tiempo de fluoroscopia y adoptar sistemas de protección a nivel del globo ocular.

(Sometido por Rafael Villavicencio, MD)

PROTECCION MIOCARDICA CON CARDIO- PLEJIA EN LA CORRECCION COMPLETA DE LA TETRALOGIA DE FALLOT

Núñez, L., Iglesias, A., Gil-Aguado, M., et al. *Rev. Esp. Cardiol.* 32 (5): 411, 1979.

Se presentan los resultados obtenidos en 32 pacientes consecutivos sometidos a reparación completa de la Tetralogía de Fallot utilizando cardioplejia para proteger el miocardio. La solución estaba compuesta de: 20 meg. KCL; 20 meg. NaHCO₃, 25 gm. de manitol y dextrosa al 5 por ciento hasta completar 500 cc. Las edades fluctuaron de los 2 a 16 años y quince de ellos tenían algún tipo de anastomosis aorto-pulmonar previa. La mortalidad operatoria fue de 0 por ciento y no hubo casos de bajo volumen minuto excepto en un paciente con una comunicación interventricular residual.

La tetralogía de Fallot abarca un amplio espectro anatomo-patológico y funcional lo que complica, hace difícil, o no permite una verdadera corrección total de la malformidad. En estos casos el uso de cardioplejia reduce la mortalidad y morbilidad por bajo gasto cardíaco.

(Sometido por Rafael Villavillencio, MD)

STRATEGIES IN THE TREATMENT OF SYSTEMIC FUNGAL INFECTIONS

G. Medoff and G. S. Kobayashi - *New Engl. J. Med.* 302: 145, 1980.

Un repaso del uso de agentes antihongos tales como amfotericina B, nystatina, filipina, clotrimazole, miconazole, ketonazole, flucytosina e iodo.

El concepto de combinación de agentes se discute. Una buena lectura y excelente referencia.

(Sometido por Carlos H. Ramírez Ronda, MD)

THE USE OF LETHIUM CARBONATE TO REDUCE INFECTION AND LEUKOPENIA DURING SYSTEMIC CHEMOTHERAPY

Lyman, G.H., et al. *New Eng. J. Med.* 302: 257, 1980.

El carbonato de litio induce leucocitosis inocua e irreversible en pacientes psiquiátricos. Se ha sugerido que el litio puede ser capaz de disminuir la leucopenia asociada con quimioterapia.

Se realizó un estudio de 45 pacientes con carcinoma del pulmón recibiendo quimioterapia. Se le administró a 20 pacientes carbonato de litio 300 mg tres veces al día durante el período de inducción y por 48 hrs. post quimioterapia. Los pacientes que recibieron litio tuvieron menos días con neutropenia, menos días con fiebre y neutropenia y menos muertes relacionadas a infección.

El carbonato de litio puede que se utilice en el futuro en este tipo de paciente.

(Sometido por Carlos H. Ramírez Ronda, MD)

SEXUAL TRANSMISSION OF HEPATITIS A IN HOMOSEXUAL MEN: INCIDENCE AND MECHANISM

Corey, Land K. L. Holmes, *New Eng. J. Med.* 302: 435, 1980

Hepatitis A se añade a otras enfermedades sexualmente transmitidas, tales como hepatitis B, herpes genitalis, uretritis no específica, gonorrea, sífilis, chancroide, tricomoniasis, etc. La incidencia anual de hepatitis A determinada por el desarrollo de anticuerpos fue de 22 por ciento en homosexuales comparados con un grupo de heterosexuales que fue 0.

(Sometido por Carlos H. Ramírez Ronda, MD)

**CHOLERA — A POSSIBLE ENDEMIC FOCUS
IN THE UNITED STATES**

Blake, P. R., et al. *New Engl. J. Med.* 302: 305, 1980

Cólera es una infección clásicamente considerada de la región asiática, con una pandemia que comenzó en 1961 y que ha llegado hasta Europa; se ha mantenido

fuera del nuevo mundo.

En la región del Golfo de los Estados Unidos se han descrito 11 casos en donde se recobró *Vibrio Cholerae* O-grupo 1, en personas que comieron cangrejos. Esto indica que el *Vibrio Cholerae* está presente y persiste en el Golfo de los Estados Unidos.

(Sometido por Carlos H. Ramírez Ronda, MD)

CORONARY CARE

compiled by L. Julian Haywood, MD and Melvin M. Scheinman, MD

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NOTICIAS

STATEMENT OF THE AMERICAN MEDICAL ASSOCIATION TO THE FOOD AND DRUG ADMINISTRATION ON INFANT FORMULAS - February 19, 1980

Mr. Chairman:

My name is Gilbert B. Forbes, MD. I am a physician, Board Certified in Pediatrics, and currently serve as Chief Editor of *The American Journal of Diseases of Children*. With me today are Philip White, Sc.D., Director of AMA's Department of Foods and Nutrition, and Nancy Cahill, of AMA's Department of Federal Legislation.

I am pleased to present the views of the American Medical Association with respect to both recent and recurring questions regarding infant formulas and infant nutrition generally. It is fitting that the AMA witness is the Chief Editor of *The American Journal of Diseases of Children* to speak on its behalf today inasmuch as the *Journal* has chronicled the development of infant formulas for almost seventy years. The triumphs and the troubles encountered with these products have been, and continue to be, communicated to practicing physicians by these AMA publications.

The Food and Drug Administration's purpose in calling this public meeting is to gather information and informed views on issues surrounding the manufacture, labeling, and need for clinical testing of infant formulas. Deferred, until March 1980 hearings, are questions regarding the composition of infant formulas. We will limit our remarks here accordingly, with the understanding that much of what we say about the issues being discussed today bears directly on questions that will be addressed next month regarding the need to revise the existing regulation on nutrient composition of infant formulas.

Clinical Experience with Infant Formulas

AMA supports the American Academy of Pe-

diatrics recommendation that full term infants should be breast-fed, unless there are specific contraindications or breast-feeding is unsuccessful. For such circumstances, physicians have a variety of proprietary infant formulas available. The paramount concern of the AMA with respect to these products is that physicians prescribing (and parents using) an infant formula have confidence in the suitability of the formulation. This confidence must be based on a number of assurances not directly under the control of physician or parent:

1. appropriate nutritional composition and value;
2. product safety; and
3. acceptability of the product to the infant.

Today, the physician has reason to be confident in prescribing infant formulas. Clinical experience gained over the years, along with information continually being made available by the manufacturers, has strengthened the conviction that physicians can prescribe these products with confidence. Such was not always the case.

The infant formulas of today evolved through 120 years of research and *clinical experience*, which, parenthetically, must be distinguished from *clinical testing* for the purposes of today's discussions. The American Medical Association, through the work of its Council on Foods and Nutrition (1929-1954), participated in the evolution of these formulas. During the period from 1930 to 1954 for example, the Council on Foods and Nutrition conducted its Seal of Acceptance Program.

During this time, this Council had established a set of rules, regulations and general decisions to use in the evaluation of infant formulas. A "Seal of Acceptance" was granted a formula for a two-year period if it met the appropriate standards. After two years, each

product was completely re-evaluated. Naturally, the criteria for acceptance changed as the science of infant feeding progressed. The most striking advances were in the realm of scientific innovation. In the earliest days of the Council's program, for example, infant formulas were developed largely by empirical manipulation of cows' milk and some sources of carbohydrates and fats. The resources and processes involved reflected the state-of-the-art at the time. By the time the Seal of Acceptance Program was terminated in 1954, however, infant formula manufacturing had reached a significant degree of sophistication. Today, we are increasingly looking to what might seem unusual sources, such as the soybean, for a base of infant nutrition.

As the AMA's Council on Foods and Nutrition devoted less of its attention to the subject, the American Academy of Pediatrics Committee on Nutrition, organized in 1956, provided correspondingly more attention to the nurture of the infant. One of the last activities of the AMA Council in the area of infant nutrition was the sponsorship of a symposium on the subject in 1959. The titles of the papers presented illustrate the concerns at that time; and suggest how far we have come since:

- *The Amino Acid Requirements of Infants,*
- *Differences Between Cows' and Human Milk,*
- *Protein Allowances for Premature Infants,*
- *Iron Requirements in Infancy.*

This overview is not meant to suggest that the AMA has played only an historical role in infant nutrition. We are very much aware of the more recent questions and controversies regarding infant nutrition generally and infant formulas specifically. Close liaison between the AMA and the American Academy of Pediatrics, as well as with FDA, is still maintained.

Mr. Chairman, recent years have seen unparalleled growth in our knowledge of infants' nutritional requirements. This knowledge has guided the development of standards of composition for infant formulas and has clarified concepts of uses of the various ge-

neric formulas available. The net result—to the credit of all parties involved—has been that no nutritional deficiencies have been reported when infants have been fed formulas that met the standards developed by the Academy.

AMA Recommendations

The physician now has available a range of infant food formulations that permit him to manage almost any feeding problems that may arise. The development of these products has been made possible by the cooperation of the medical profession and infant formula manufacturers, with the involvement of FDA and other agencies as appropriate.

While we are close to having formulas available that are acceptable in all regards, we cannot now conclude that that pinnacle has been reached. Continuing research in the realm of infant nutrition is essential, and product development must continue to keep pace with this research.

On the other hand, we are equally concerned that these products cannot provide the benefits they promise if they are unavailable—whether made so by cost considerations or government intervention. We sincerely hope that overreaction to recent, isolated problems will not be permitted to call forth unnecessary and undesirable legislation or regulation. Governmental overreaction would serve only to unduly disturb patients of infants using safe and nutritious formulas, increase the cost of these oftentimes essential substitutes for mother's milk, and seriously inhibit further advances in infant nutrition and formula design.

Mr. Chairman, the AMA shares the concern expressed by FDA Commissioner Jere Goyan, as stated in his October 31, 1979 press release, that FDA and other responsible parties be careful to "[convey] the proper sense of concern" with respect to both the immediate problems encountered with infant formulas and the longer term solutions under discussion. We believe that FDA, the infant formula manufacturers, and representatives from physician and consumer groups can and should begin immediately to work together to devise voluntary initiatives to enhance the reliability of and consumer confidence in infant formulas being marketed.

We are particularly interested in voluntary initiatives being undertaken to improve post-market clinical monitoring, product surveillance and reporting. Given the state-of-the-art of infant nutrition today, the information generated by improved monitoring and surveillance activities, evaluated in the context of decades of clinical experience, could be far more useful than any additional, regulation-directed clinical testing of infant formulas. In this case, we agree philosophically with President Carter's directive that prior to government intervention, it is best to seek solutions in the private sector.

Conclusion

Clinicians and consumers in this country have every reason to expect each manufacturer of infant formulas to conduct all product and process testing necessary to assure the safety, nutritional adequacy, and acceptability of any infant formula marketed here or abroad. They have a right to expect product labeling to contain all of the information necessary to permit the proper use of each product. However, it is also proper that we recognize the significant contributions today's infant formula manufacturers have made to infant nutrition — while compiling an enviable safety record.

Mr. Chairman, the AMA believes that the public can have justifiable confidence in the infant formula products marketed in this country today. In the course of ensuing discussions, we would hope that this message is given the prominence it deserves and that it engenders the regulatory restraint appropriate under the circumstances.

AMA NEWS:

IMPOTENCE OFTEN HAS PHYSICAL CAUSE, DOCTOR DECLARES

CHICAGO - Physicians have been taught for many years that impotence in their male patients is almost always caused by emotional imbalance and very seldom has a physical cause.

A Harvard Medical School research project challenges this theory in the Feb. 22-29 Journal of the American Medical Association. Possibly one-third of those men thought to be impotent from emotional reasons actually have a physical problem that is causing their inability to perform sexually, says Richard F. Spark, MD, of Boston.

Dr. Spark performed tests to determine the level of the sex hormone testosterone in 105 impotent men. He found that 37 of the men had previously unsuspected glandular disorders. Once the disorder was discovered, appropriate treatment was begun, and potency was restored to 33 of the 37, he says.

Erectile potency depends not only on a healthy psyche, but also on intact neurological, vascular and hormonal systems, Dr. Spark points out.

All of the men in the study had been receiving regular medical care from their own physicians. When impotence was discussed, the patients were told that it was either a result of the natural process of aging ("after all, you're not 21 any more") or a manifestation of anxiety or depression. This is the conventional medical wisdom on the subject. Hormonal tests were not performed.

Says Dr. Spark:

"Recent advances in endocrinology (study of glands) and the experience cited here indicates that the time may be propitious for us to restructure our approach to the impotent patients. The association of an unsettling life event and the development of impotence need not imply a cause-and-effect relationship. Developing impotence is, by itself, sufficient cause for depression and would understandably stress otherwise stable relationships."

DEATH OF THOUSANDS PREDICTED FROM ASBESTOS EXPOSURE

CHICAGO — During the next 40 years, an average

of 20,000 deaths per year will result from asbestos exposure, and very little is being done to prevent it, says a report in the Jan. 18 Journal of the American Medical Association.

Dr. Irving J. Selikoff, director of the Environmental Sciences Laboratory at Mount Sinai School of Medicine in New York, told the JAMA Medical News section that "In the period between World War II (when asbestos use first became widespread) and the end of this century, well over a half a million Americans will have died of asbestos-related diseases."

Aside from "meager attempts to regulate new asbestos use and to monitor occupational exposure, virtually nothing is being done to remedy the public health failure and turn back the legacy of death from asbestos," the JAMA article says.

Some 700,000 tons of asbestos is still being used annually in the United States to make products such as cement pipe, brake linings, asbestos paper products, and textiles. Virtually no precautions other than a maximum exposure standard for workers that some consider unacceptably high are being taken to prevent asbestos-related disease, the report says.

"Unless we learn the lessons of the past," predicts Dr. Selikoff, "we are destined to compound the deadly legacy of asbestos and start the clock ticking for the next 40 years."

There is no truly effective treatment for any of the asbestos-related diseases, which include asbestosis, mesothelioma (a form of cancer), cancer of the lung and some cancers of the esophagus, stomach or colon-rectum. A long period of development (25 to 30 years in most cases), difficulty in diagnosis, and the lack of any widely applied long-term surveillance mechanism all spell a grim outcome for the asbestos-exposed population, JAMA declares.

The epidemic of asbestos-related disease is a public health failure rather than a failure of the medical profession, Dr. Selikoff declares. The substance is in buildings, schools, homes and cars, and "we have made an unconscious decision to accept some level of mortality as the price we must pay for its usefulness."

As for whether there is any "safe" level of exposure to asbestos, experts such as David P. Rall, MD, Director of the National Institute of Environmental Health Sciences, Philip E. Enterline, Ph.D., of the Uni-

versity of Pittsburgh, and Dr. Selikoff believe there is not. Scientists at the Environmental Protection Agency (EPA) concur.

The EPA in fact is contemplating placing a ban on the commercial use of asbestos. There are now a number of substitutes for the substance although the asbestos industry claims that few are as good.

The only way to eliminate asbestos diseases is to eliminate asbestos exposure, the article concludes.

MEDICATION FOUND EFFECTIVE IN TRAVELER'S DIARRHEA

CHICAGO — Another medication to control traveler's diarrhea has proved effective for many individuals, says a research report in the Jan. 16 Journal of the American Medical Association.

The product is subsalicylate bismuth. Dr. Herbert L. DuPont of the University of Texas Medical School, Houston, reports on a trial of the drug among American students attending summer classes in Guadalajara, Mexico.

Seventy-five students received subsalicylate bismuth four times daily. The other 75 received placebos. Diarrhea developed in 14 of the students receiving the drug, but 40 of the students taking the placebo became ill.

The protective effect was apparent within a day or two of the beginning of the study, Dr. DuPont says. The treated students experienced fewer intestinal complaints and were less likely to pass soft or watery stools, he found.

In an accompanying editorial, Dr. Sherwood L. Gorbach of Tufts-New England Medical Center, Boston, points out that "Certainly, there will be other advances in this field, but the subsalicylate bismuth regimen is the first to offer safe prophylaxis to the beleaguered wayfarer who suffers the intestinal agonies of foreign travel."

Dr. Gorbach points out that one problem would be a supply of the drug. Approximately half a pint daily was used in the Mexican experiment. This would require that the traveler on a three-week trip to Mexico carry 21 bottles of the drug.

"An extra suitcase would perhaps suffice, and this would permit additional room on the return trip for souvenirs."

WOMEN HAVE NATURAL IMMUNITY TO DISEASES THAT STRIKE MEN

CHICAGO — Who says women are the weaker sex? Two physicians writing in the American Medical Association's *Journal of Diseases of Children* present evidence that females are naturally immune to certain diseases.

David T. Purtilo, MD and John L. Sullivan, MD, write that "Evolutionary selection has equipped females with immunoregulatory genes on the X chromosome for coping with life-threatening illnesses. Females, who have one more X chromosome than males, are less likely to get some infectious diseases and certain forms of cancer."

Through the life cycle, males show a decreased survival rate. Although there are five per cent more male babies born than females, that number diminishes until, in later life, women outlive men by eight years. Some explanation for this mortality rate lies in environmental exposure.

"In addition to accidents, severe infectious diseases are responsible for many deaths in males. Severe respiratory infections with parainfluenza show male preponderance."

Studies show that males experience more staph infections and, during recent epidemics of Legionnaires' disease, three times more men than women fell victim to it.

There are genes on the X chromosome that make

females more immune to these diseases. By having two X chromosomes, females have a natural survival advantage over males.

MODEL STATE ACT DRAFTED TO DEFINE WHEN DEATH OCCURS

CHICAGO — The American Medical Association has forwarded model legislation to state medical associations which would define when a person is dead.

The model act declares: An individual who has sustained either (1) irreversible cessation of circulatory and respiratory functions, or (2) irreversible cessation of functioning of the entire brain, shall be considered dead. A determination of death by a physician shall be made only in accordance with accepted medical standards.

The model death bill was first adopted a year ago, and was amended in December by the AMA House of Delegates at its interim winter meeting in Honolulu.

There are now 25 states that already have adopted some form of legislation concerning brain death, said Richard Krause of the AMA's Department of State Legislation. The new bill is offered to all states however, should some of those with present laws wish to consider changes or amendments.

The statement of when death occurs is intended to provide a comprehensive statement for declaring death in all situations, codifying common law regarding death based on cardiorespiratory cessation, and clarifying the law regarding brain death as an acceptable basis for determining death, Mr. Krause said.

The model act, if adopted by state legislatures, will facilitate the obtaining of organs from individuals who have just died for transplantation into living persons with failing organs. Kidney transplants are now

routine, and numerous other organs sometimes are transplanted.

PARAMEDIC TREATMENT OF CARDIAC ARREST OFFERS BETTER RESULTS, STUDY SHOWS

CHICAGO — The sophistication and cost of paramedic services in the treatment of cardiac arrest has been superior to services offered by Emergency Medical Technicians, a study reported in the *Journal of the American Medical Association* reveals.

Survival after out-of-hospital cardiac arrest treated by EMTs with basic life supports was studied in four communities with a combined population of 380,000.

During the two-year period studied in King county (Seattle) 18 or 6 per cent of 321 patients with cardiac arrest were resuscitated and ultimately discharged from the hospital.

This figure was in contrast to 55 or 22 per cent of 253 discharged in adjacent suburban communities with paramedic services.

The evident factor, according to the article, accounting for the difference in survival rates was the time from collapse to receiving definitive care (advanced cardiac life support) — 26 minutes in the EMT area compared to 7.8 minutes in the paramedic area.

In comparing the two services, the report, compiled by Mickey S. Eisenberg, MD, Michael K. Copass, MD, Alfred Hallstrom, PhD, Leonard A. Cobb, MD, and Lawrence Bergner, MD, explains that the EMTs are usually regular members of fire or police departments or commercial ambulance companies and therefore add little or no cost to existing activities. The more fundamental emergency medical technicians (EMTs) receive a standard 80-hour course in basic medical emergency care and can perform cardiopulmonary resuscitation (CPR), but not defibrillation, endotracheal intubation or administration of medications.

The paramedics on the other hand, the article points out, are highly trained personnel who have received up to 1500 hours of training and can administer such advanced emergency care as defibrillation, endotracheal intubation and parenteral cardiac medications.

And considerable evidence exists, the article points out, that paramedics can resuscitate people in cardiac arrest, particularly ventricular fibrillation.

While there have been proposals to provide additional training and skills for EMTs, there has been little definition of what skills are most important and thus little basis for deciding whether intermediate services between the EMTs and the paramedics can be effective.

Commenting on the results of the study, it was pointed out that successful outcome after cardiac arrest is associated with minimal delay to initiation of CPR and provision of definitive care. Both factors are important, it is explained, and one without the other is unlikely to result in survival.

For the EMT treated patients, the time to definitive care was considerably longer because patients had to be transported from the scene with ongoing CPR to the hospital for definitive care.

The options to shorten the time to definitive care range from the ludicrous (a hospital on every street corner) to the expensive (paramedic services in every community). An option that may hold some promise, the article states, is training EMTs to recognize ventricular fibrillation prior to the onset of severe hypoxia and acidosis.

MEDICAL SCHOOL ENROLLMENT HITS NEW PEAK, AMA REPORTS

CHICAGO — Total enrollment in the 125 U. S. medical schools in 1978-79 was 62,754, an increase of 2,804 over the previous year, says the American Medical Association's 79th annual report on medical education, published in the March 7 *Journal of the*

American Medical Association.

For the second successive year the AMA noted a significant downturn in the number of applicants to medical schools, said C. H. William Ruhe, MD., senior vice president for scientific affairs. The 1978-79 applicant total was 36,636, a drop of almost 4,000 from the previous year, and down from the peak year of 42,624 applicants in 1974-75.

There still were 2.2 applicants for each place in the freshman class. New enrollment totaled 16,620 students in 1978-79, an increase over the previous year's total of 16,134.

The medical schools graduated a record number of new physicians at the close of the 1978-79 year, 14,966, an increase of 4 per cent over the previous year.

The total number of women enrolled in medical schools continued to climb, to 15,293, an increase of 920 over 1977-78. Some 24.4 per cent of medical students are women.

Ethnic minorities enrolled in medical schools in 1978-79 totaled 7,768, a percentage of 12.5.

Dr. Ruhe noted that "Again the trend at both the federal and state level is in the direction of increasing regulation of the medical education system, increasing dictation of the terms of medical education and the content of the curriculum, and increasing regulation of the nature and location of physicians' practices."

At the federal level, he said, the movement of legislative support was away from medical education.

"In general, Congress is persuaded that the supply of physicians is now adequate and that financial support for schools of medicine may be reduced safely."

At the state level, there were efforts to restrict licensure of new physicians in two states, and other proposals to limit the numbers of new residency programs, as states feared an over-supply of doctors or a relative imbalance between primary care physicians and secondary/tertiary care physicians.

CHICAGO — The American Medical Association this spring continues its long standing program to urge Americans not to smoke.

In a report: "Smoking and Health", in the Feb. 22-29 Journal of the American Medical Association, the AMA's Council on Scientific Affairs calls on doctors to move still more into the forefront of the campaign against tobacco.

Those few remaining physicians who continue to smoke (most have quit) are urged by their peers in the AMA to stop, as an example to their patients, and for the sake of their own health. Doctors are urged to discourage smoking among their patients, to alert smokers to the health hazards, to place "No Smoking" signs in their waiting rooms and to discourage smoking in hospitals where they work.

The AMA urged national, state and local medical and specialty societies to encourage their members to more vigorous antismoking efforts. The AMA also encourages Congress to pass laws readjusting the cigaret tax, phase in the production of less toxic and hazardous tobacco, and make the health warning on cigaret packs more explicit.

Stricter regulation of tobacco advertising is urged of the Federal Trade Commission. Educational programs in schools are encouraged, and insurance companies are urged to make available to nonsmokers health and other policies at reduced rates.

The Council declares:

"There remains no doubt that the morbidity and mortality (disease and death) in cigaret smokers are in excess over that seen in nonsmokers. This is caused by arteriosclerotic heart disease, chronic pulmonary disease, cancers of the respiratory tract, and the syndrome of sudden death, and is associated with cancer of the bladder, kidneys and pancreas, as well as peptic ulcers.

"Tobacco smoke will account for 346,000 deaths this year in the United States."

AMA STEPS UP LONG CAMPAIGN TO DISCOURAGE SMOKING

AMA HEALTH AND SAFETY TIPS

ALCOHOL & DRUGS

Drinking and driving don't mix. Drinking alcohol while you're taking tranquilizers or sedatives can be hazardous.

No doubt you've heard these warnings before. But, according to the American Medical Association, there are many dangerous combinations of drugs and alcohol that are not as commonly known

For example, aspirin is a stomach irritant to begin with; taking it with alcohol will aggravate the condition. An anticonvulsant, used to control epilepsy, can be negated by excessive drinking, and seizures could result. Taking liquor and an antihistamine can be especially dangerous, if you drive. The antihistamine present in even a nonprescription cold remedy often causes drowsiness, but that effect is exaggerated by drinking.

These combinations, of course, are not as harmful as mixing alcohol and tranquilizers, but they can have serious effects nonetheless. Don't be fooled into thinking that only heavy drinkers will suffer these ill effects; a moderate intake of alcohol does not mix any better.

ALCOHOL & DRUGS

No doubt you've heard warnings about the harmful combination of alcohol and tranquilizers. But, according to the American Medical Association, there are many dangerous combinations of drugs and alcohol that are not as commonly known — including many "harmless" over-the-counter pain and cold remedies. Certain effects of preparations containing aspirin or antihistamines are greatly exaggerated when mixed with alcohol—even in moderate amounts.

STRESS

Stress..... most of us encounter it everyday. Too much bad news, problems at work, money worries,

even a change in sleeping habits are stress factors that may be overwhelming. According to the *Journal of the American Medical Association*, stress is what happens when the body's vital functions are subjected to wear and tear beyond their ability to balance.

When your body reaches its capacity for handling stress, a variety of physical symptoms may appear — headache, stiff neck, even a toothache from clenching your jaws.

A certain amount of stress, however, is not bad for you. We couldn't handle life's daily demands if the body were not stimulated by a healthy amount of tension.

There are some actions you can take when you suspect your backache or stiff neck is due to stress: take a long walk or get involved in physical activity such as running or swimming; talk out your problem with a friend or co-worker; and recognize what is troubling you and accept what you can't change.

STRESS

Stress.... most of us encounter it everyday. According to the *Journal of the American Medical Association*, stress is what happens when the body's vital functions are subjected to wear and tear beyond their ability to balance. When physical symptoms such as backache or stiff neck appear and you think they may be stress-related, channel your energies into a physical activity instead of worrying about them.

DRUG INTERACTIONS

Many commonly prescribed drugs, when mixed with other drugs or food, can have reactions that may

surprise you, says the American Medical Association. While anti-inflammatory drugs are often taken with milk, some antibiotics *should not*. Even aspirin can exaggerate or decrease the effects of a drug. Check with your physician or pharmacist if you're in doubt about what you're taking.

DRUG INTERACTIONS

Many commonly prescribed drugs — and even certain over-the-counter medications — may have some surprising reactions when mixed with foods or other drugs. The American Medical Association recommends

carefully reading the label on all prescription and nonprescription drugs and checking with your family physician before taking any combination of drugs.

Anti-inflammatories are often taken with milk or food because they may irritate the stomach, while some antibiotics *should not* be taken with milk, since the calcium in milk inhibits the absorption of the drug.

Simple nonprescription drugs such as antacids and even vitamin supplements with iron can decrease the effectiveness of some antibiotics. And aspirin can exaggerate the effects of other prescription drugs.

It's helpful if you keep your physician informed of any medication you take so he or she may keep a complete record. If you regularly take over-the-counter medications, your doctor should know what they are.

A N U N C I O S

Por razones de salud: Vendo esquina comercial "1" con estructura de hormigón. Excelente para oficina de doctores. Laboratorio clínico, Rayos X, farmacia, etc. Cabida: 490 Mts² solar. Localización Ave. Ponce de León, Frente Edificio General Computer, Area de Río Piedras. Para información llamar: tel. 767-1394 después 4:00 p.m.

Locales para oficinas médicas localización colindante con Hospital San Martín, comunicarse con el Sr. Robles, 1028 Calle Los Angeles, Urb. del Carmen, Río Piedras, tel. 751-4319.

ELECTROCARDIOGRAM OF THE MONTH

This electrocardiogram (ECG), Figure 1, is from an 18-year-old male with marked cardiomegaly.

Diagnosis:

1. Describe the ECG.
2. What is your diagnosis?
3. What is the pathogenesis of this pattern?

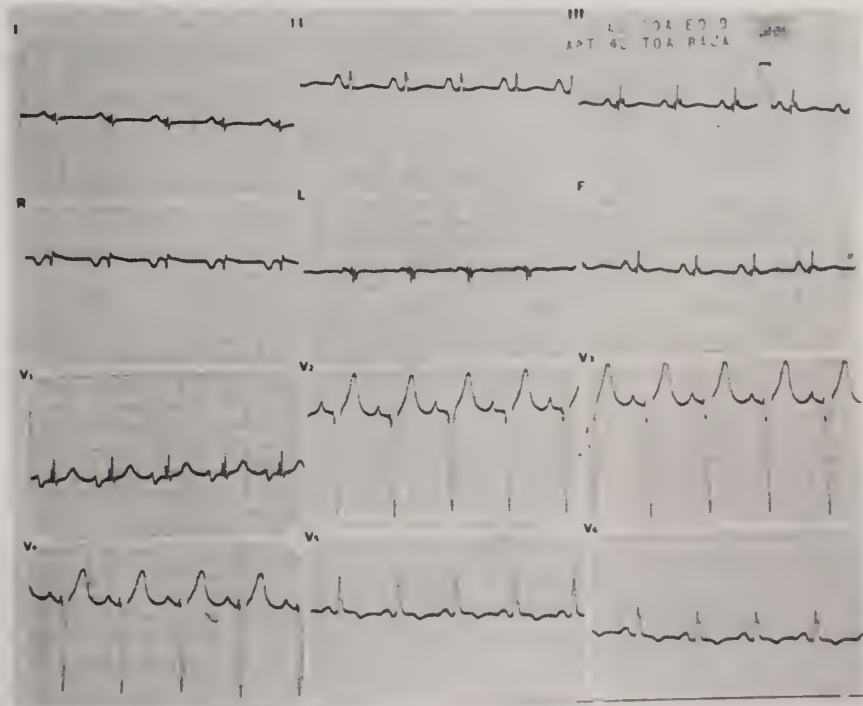


Figure 1: Duchenne's Muscular Dystrophy

Answer

Duchenne's Muscular Dystrophy.

Clue: He was observed sitting in a wheelchair!

There is a sinus tachycardia of 112. The P waves are large and peaked in leads 11, aVR, aVF and V₁₋₄. The QRS complexes are multiphasic. A qrsR's complex is seen in V₁ and slurred rS (small r) complexes in V₂₋₄. The T waves are low in lead 1, inverted in V₅₋₆, upright and prominent in V₁₋₄. The study is compatible with biatrial enlargement, incomplete right bundle branch block, anterior myocardial infarction (MI) and T wave abnormalities.

Muscular dystrophy, especially Duchenne's, manifests an early typical pattern of right ventricular hypertrophy and posterolateral MI (or inferior MI) by tall R waves in the right precordial leads and deep Q's in the left precordium and inferior leads. Persistent sinus tachycardia, a short P-R interval, P abnormalities conduction defects and nonspecific ST-T abnormalities may be present. Changes may be observed even in family members and asymptomatic female carriers. The pseudo-MI patterns have been explained by vacuolization, fragmentation, necrosis, fibrosis and scarring of multiple areas, particularly the posterior-lateral basal region of the left ventricle. An arteriopathy of the small arteries to the sino-atrial and atrioventricular nodes with degeneration of the former has been described. The ECG, ballistocardiogram and echocardiogram (relaxation abnormality of posterior left ventricular wall) are the earliest and most sensitive indicators of cardiac involvement; the ECG is abnormal in 40-90 per cent of patients with Duchenne's Muscular Dystrophy.

Charles D. Johnson, MD
UPR School of Medicine
Dept. of Medicine

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1. Committee on Nutrition: Commentary on breast feeding and infant formulas, including proposed standards for formulas. *Ped* 52:278-285, 1976.

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In diagnosing work-related musculoskeletal disorders, such as low back pain, it is often helpful to have the patient simulate the motions he does at work.

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clinical studies have shown that patients respond by the first evaluation period (day 2)^{6,7}

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VA 6505-00-764-3313A

Summary of Prescribing Information

***Indications:** Based on a review of this drug by the National Academy of Sciences-National Research Council and/or other information, FDA has classified the indications as follows:
"Probably" effective as an adjunct to rest and physical therapy for the relief of discomfort associated with acute, painful musculoskeletal conditions. The mode of action of this drug has not been clearly identified, but may be related to its sedative properties. Chlorzoxazone does not directly relax tense skeletal muscles in man.

Contraindications: Sensitivity to either component

Warnings: Usage in Pregnancy—Use in women of childbearing potential only when potential benefits outweigh possible risks.

Precautions: Exercise caution in patients with known allergies or history of drug allergies. If a sensitivity reaction or any signs or symptoms suggestive of liver dysfunction are observed, the drug should be stopped.

Adverse Reactions: Occasionally, drowsiness, dizziness, light-headedness, malaise, overstimulation or gastrointestinal disturbances may be noted; rarely, allergic-type skin rashes, petechiae, ecchymoses, angioneurotic edema or anaphylactic reactions. In rare instances, chlorzoxazone may possibly have been associated with gastrointestinal bleeding. While PARAFLEX[®] (chlorzoxazone) tablets and other chlorzoxazone-containing products have been suspected as being the cause of hepatic toxicity in approximately twenty-seven patients, it was not possible to state that the dysfunction was or was not drug induced.

Usual Adult Dosage: Two tablets q.i.d.

Supplied: Light green tablets, imprinted "McNEIL" and "PARAFON FORTE"—bottles of 100 and 500.

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For information on symptoms/treatment of overdosage, see full prescribing information.

PARAFON FORTE tablets are manufactured by McNeil Laboratories Co., Dorado, PR 00646.

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- As part of HDPF's systematic treatment and follow-up program, the primary step-1 agent was chlorthalidone: Hygroton.²

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in an effective low dose**

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BRIEF SUMMARY

Indications: Hypertension, adjunctive therapy in edema. **Contraindications:** Anuria, hypersensitivity to chlorthalidone or other sulfonamide-derived drugs. **Warnings:** Should be used with caution in severe renal disease, impaired hepatic function or progressive liver disease. May add to or potentiate the action of other antihypertensive drugs. Sensitivity reactions may occur in patients with a history of allergy or bronchial asthma. There is a possibility of exacerbation or activation of systemic lupus erythematosus with thiazides, which are related to chlorthalidone. This has not been reported with chlorthalidone. Thiazides cross the placental barrier and appear in cord blood. Use in pregnant women requires that the anticipated benefits of the drug be weighed against possible hazards to the fetus. These hazards include fetal or neonatal jaundice, thrombocytopenia, and possibly other adverse reactions which have occurred in the adult. In nursing mothers, thiazides cross the placental barrier and appear in breast milk. If use of the drug is essential, the patient should stop nursing. **Precautions:** Periodic determination of serum electrolytes to detect possible electrolyte imbalance should be performed at appropriate intervals. All patients receiving chlorthalidone should be observed for clinical signs of fluid or electrolyte imbalance, namely, hyponatremia, hypochloremic alkalosis, and hypokalemia. Serum and urine electrolyte determinations are particularly important when the patient is vomiting excessively or receiving parenteral fluids. Medication such as digitalis may also influence serum electrolytes. Hypokalemia may develop with chlorthalidone as with any other potent diuretic, especially with brisk diuresis, when severe cirrhosis is present, or during concomitant use of corticosteroids or ACTH. Interference with adequate oral electrolyte intake will also contribute to hypokalemia. Digitalis therapy may exaggerate metabolic effects of hypokalemia especially with reference to myocardial activity. Any chloride deficit is generally mild and usually does not require specific treatment except under extraordinary circumstances (as in liver disease or renal disease). Dilutional hyponatremia may occur in edematous patients in hot weather. Hyperuricemia may occur or gout be precipitated in certain patients. Insulin requirements in diabetic patients may be increased, decreased, or unchanged and latent diabetes mellitus may become manifest. Chlorthalidone and related drugs may increase the responsiveness to tubocurarine. The antihypertensive effects of the drug may be enhanced in the postsympathectomy patient. Chlorthalidone and

related drugs may decrease arterial responsiveness to norepinephrine. If progressive renal impairment becomes evident, as indicated by a rising nonprotein nitrogen or blood urea nitrogen, a careful reappraisal of therapy is necessary with consideration given to withholding or discontinuing diuretic therapy. Chlorthalidone and related drugs may decrease serum PBI levels without signs of thyroid disturbance. **Adverse Reactions:** Anorexia, gastric irritation, nausea, vomiting, cramping, diarrhea, constipation, jaundice (intrahepatic cholestatic jaundice), pancreatitis, dizziness, vertigo, paresthesias, headache, xanthopsia, leukopenia, agranulocytosis, thrombocytopenia, aplastic anemia, purpura, photosensitivity, rash, urticaria, necrotizing angitis (vasculitis) (cutaneous vasculitis), Lyell's syndrome (toxic epidermal necrolysis). Orthostatic hypotension may occur and may be aggravated by alcohol, barbiturates or narcotics. Other adverse reactions include hyperglycemia, glycosuria, hyperuricemia, muscle spasm, weakness, restlessness, impotence. Whenever adverse reactions are moderate or severe, chlorthalidone dosage should be reduced or therapy withdrawn. **Usual Dose:** One tablet daily. **How Supplied:** Tablets—100 mg. (white, scored), 50 mg. (aquea) in bottles of 100, 1000 and 5000; 25 mg. (peach) in bottles of 100 and 1000; unit-dose blister packs, boxes of 100 (10 x 10 strips).

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Before prescribing, please consult complete product information, a summary of which follows:

Indications: Relief of anxiety and tension occurring alone or accompanying various disease states. Efficacy beyond four months not established by systematic clinical studies. Periodic reassessment of therapy recommended.

Contraindications: Patients with known hypersensitivity to the drug.

Warnings: Warn patients that mental and/or physical abilities required for tasks such as driving or operating machinery may be impaired, as may be mental alertness in children, and that concomitant use with alcohol or CNS depressants may have an additive effect. Though physical and psychological dependence have rarely been reported on recommended doses, use caution in administering to addiction-prone individuals or those who might increase dosage; withdrawal symptoms (including convulsions), following discontinuation of the drug and similar to those seen with barbiturates, have been reported.

Usage in Pregnancy: Use of minor tranquilizers during first trimester should almost always be avoided because of increased risk of congenital malformations as suggested in several studies. Consider possibility of pregnancy when instituting therapy; advise patients to discuss therapy if they intend to or do become pregnant.

Precautions: In the elderly and debilitated, and in children over six, limit to smallest effective dosage (initially 10 mg or less per day) to preclude ataxia or oversedation, increasing gradually as needed and tolerated. Not recommended in children under six. Though generally not recommended, if combination therapy with other psychotropics seems indicated, carefully consider individual pharmacologic effects, particularly in use of potentiating drugs such as MAO inhibitors and phenothiazines. Observe usual precautions in presence of impaired renal or hepatic function. Paradoxical reactions (e.g., excitement, stimulation and

acute rage) have been reported in psychiatric patients and hyperactive aggressive children. Employ usual precautions in treatment of anxiety states with evidence of impending depression; suicidal tendencies may be present and protective measures necessary. Variable effects on blood coagulation have been reported very rarely in patients receiving the drug and oral anticoagulants; causal relationship has not been established clinically.

Adverse Reactions: Drowsiness, ataxia and confusion may occur, especially in the elderly and debilitated. These are reversible in most instances by proper dosage adjustment, but are also occasionally observed at the lower dosage ranges. In a few instances syncope has been reported. Also encountered are isolated instances of skin eruptions, edema, minor menstrual irregularities, nausea and constipation, extrapyramidal symptoms, increased and decreased libido—all infrequent and generally controlled with dosage reduction; changes in EEG patterns (low-voltage fast activity) may appear during and after treatment; blood dyscrasias (including agranulocytosis), jaundice and hepatic dysfunction have been reported occasionally, making periodic blood counts and liver function tests advisable during protracted therapy.

Usual Daily Dosage: Individualize for maximum beneficial effects. Oral—Adults: Mild and moderate anxiety and tension, 5 or 10 mg t.i.d. or q.i.d.; severe states, 20 or 25 mg t.i.d. or q.i.d. Geriatric patients: 5 mg b.i.d. to q.i.d. (See Precautions.)

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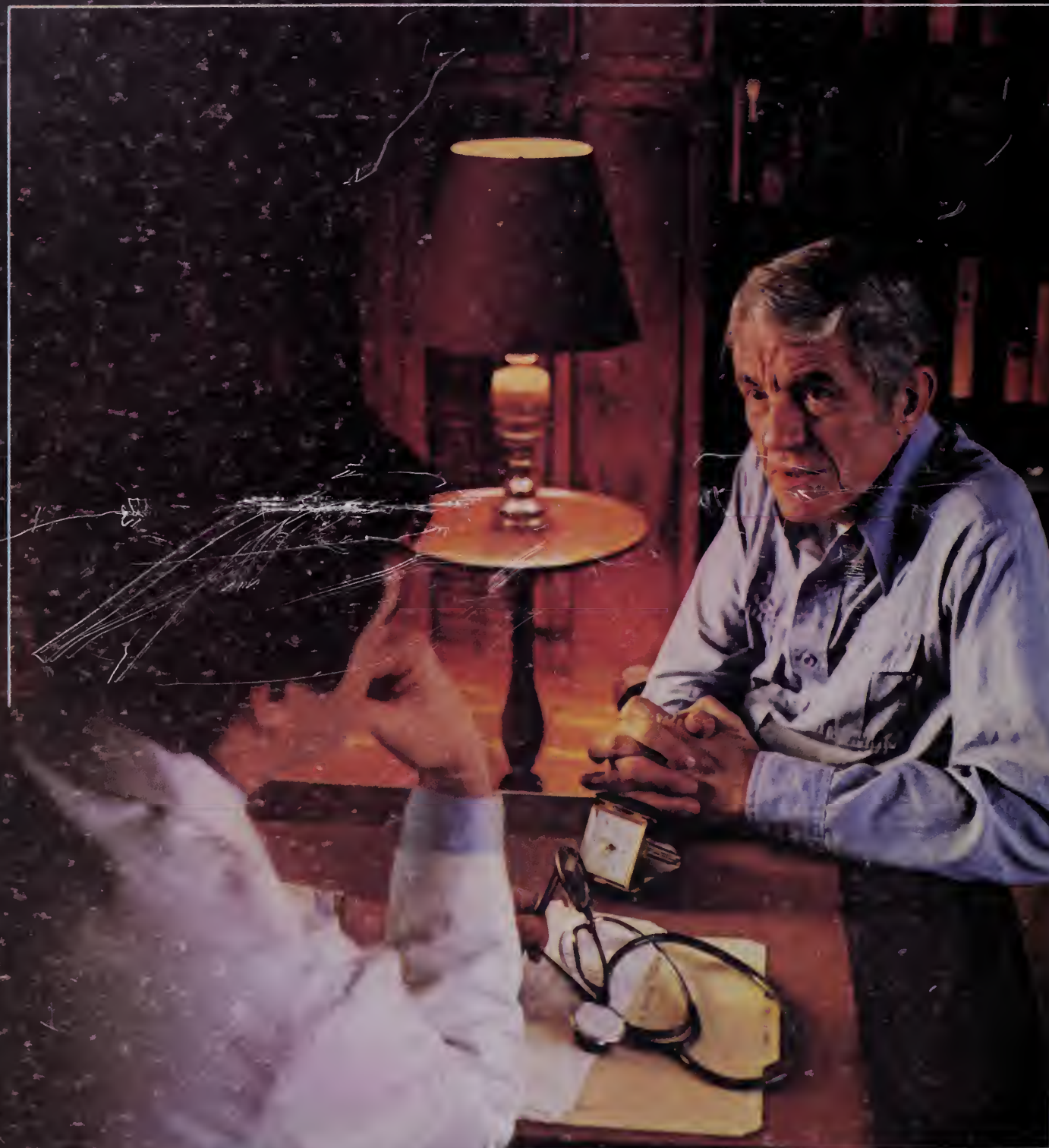
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ASOCIACION MEDICA DE PUERTORICO

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**CARDIAC PACEMAKERS, RETAINED PACEMAKER FRAGMENT AND
INFECTION - REPORT OF A CASE IN A PATIENT WITH A SUPERIOR
VENA CAVA SYNDROME**

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TWO CASES OF BECKWITH-WIEDEMANN SYNDROME, ONE WITH HEMIHYPERTROPHY

**VARIATION IN DOSE AND TIME OF COLLAGENASE DIGESTION FOR MAXIMAL
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NUM. 5

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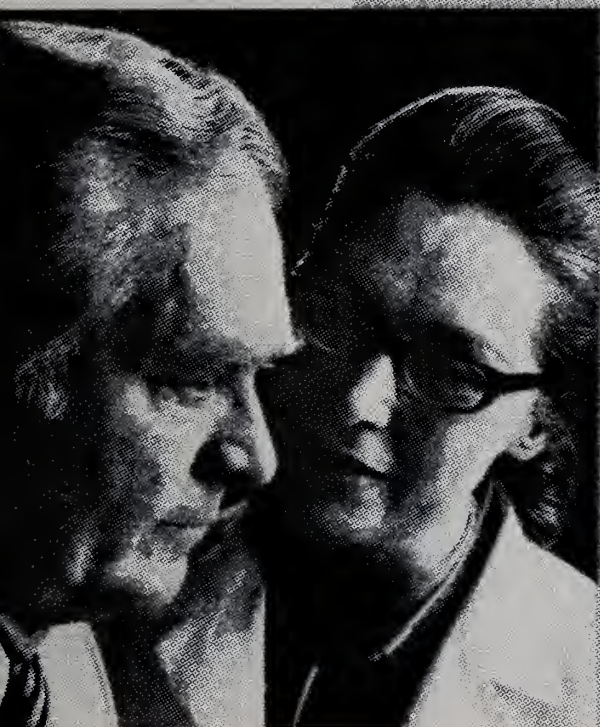
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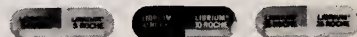




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Contraindications: Patients with known hypersensitivity to the drug.

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Usage in Pregnancy: Use of minor tranquilizers during first trimester should almost always be avoided because of increased risk of congenital malformations as suggested in several studies. Consider possibility of pregnancy when instituting therapy; advise patients to discuss therapy if they intend to or do become pregnant.

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Usual Daily Dosage: Individualize for maximum beneficial effects. *Oral—Adults:* Mild and moderate anxiety and tension, 5 or 10 mg *t.i.d.* or *q.i.d.*; severe states, 20 or 25 mg *t.i.d.* or *q.i.d.*. *Geriatric patients:* 5 mg *b.i.d.* to *q.i.d.* (See Precautions.)

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Indications: Hypertension, adjunctive therapy in edema. **Contraindications:** Anuria, hypersensitivity to chlorthalidone or other sulfonamide-derived drugs. **Warnings:** Should be used with caution in severe renal disease, impaired hepatic function or progressive liver disease. May add to or potentiate the action of other antihypertensive drugs. Sensitivity reactions may occur in patients with a history of allergy or bronchial asthma. There is a possibility of exacerbation or activation of systemic lupus erythematosus with thiazides, which are related to chlorthalidone. This has not been reported with chlorthalidone. Thiazides cross the placental barrier and appear in cord blood. Use in pregnant women requires that the anticipated benefits of the drug be weighed against possible hazards to the fetus. These hazards include fetal or neonatal jaundice, thrombocytopenia, and possibly other adverse reactions which have occurred in the adult. In nursing mothers, thiazides cross the placental barrier and appear in breast milk. If use of the drug is essential, the patient should stop nursing. **Precautions:** Periodic determination of serum electrolytes to detect possible electrolyte imbalance should be performed at appropriate intervals. All patients receiving chlorthalidone should be observed for clinical signs of fluid or electrolyte imbalance; namely, hyponatremia, hypochloremic alkalosis, and hypokalemia. Serum and urine electrolyte determinations are particularly important when the patient is vomiting excessively or receiving parenteral fluids. Medication such as digitalis may also influence serum electrolytes. Hypokalemia may develop with chlorthalidone as with any other potent diuretic, especially with brisk diuresis, when severe cirrhosis is present, or during concomitant use of corticosteroids or ACTH. Interference with adequate oral electrolyte intake will also contribute to hypokalemia. Digitalis therapy may exaggerate metabolic effects of hypokalemia especially with reference to myocardial activity. Any chloride deficit is generally mild and usually does not require specific treatment except under extraordinary circumstances (as in liver disease or renal disease). Dilutional hyponatremia may occur in edematous patients in hot weather. Hyperuricemia may occur or gout be precipitated in certain patients. Insulin requirements in diabetic patients may be increased, decreased, or unchanged and latent diabetes mellitus may become manifest. Chlorthalidone and related drugs may increase the responsiveness to tubocurarine. The antihypertensive effects of the drug may be enhanced in the postsympathectomy patient. Chlorthalidone and

related drugs may decrease arterial responsiveness to norepinephrine. If progressive renal impairment becomes evident, as indicated by a rising nonprotein nitrogen or blood urea nitrogen, a careful reappraisal of therapy is necessary with consideration given to withholding or discontinuing diuretic therapy. Chlorthalidone and related drugs may decrease serum PBI levels without signs of thyroid disturbance. **Adverse Reactions:** Anorexia, gastric irritation, nausea, vomiting, cramping, diarrhea, constipation, jaundice (intrahepatic cholestatic jaundice), pancreatitis, dizziness, vertigo, paresthesias, headache, xanthopsia, leukopenia, agranulocytosis, thrombocytopenia, aplastic anemia, purpura, photosensitivity, rash, urticaria, necrotizing angitis (vasculitis) (cutaneous vasculitis), Lyell's syndrome (toxic epidermal necrolysis). Orthostatic hypotension may occur and may be aggravated by alcohol, barbiturates or narcotics. Other adverse reactions include hyperglycemia, glycosuria, hyperuricemia, muscle spasm, weakness, restlessness, impotence. Whenever adverse reactions are moderate or severe, chlorthalidone dosage should be reduced or therapy withdrawn. **Usual Dose:** One tablet daily. **How Supplied:** Tablets—100 mg (white, scored), 50 mg (aquea) in bottles of 100, 1000 and 5000, 25 mg (peach) in bottles of 100 and 1000; unit-dose blister packs, boxes of 100 (10 x 10 strips).

References:

1. Five-year Findings of the Hypertension Detection and Follow-up Program: 1. Reduction in Mortality of Persons With High Blood Pressure, Including Mild Hypertension, JAMA 242: 2562, Dec 7, 1979. 2. Payne, G. H. Presentation of HDFP findings (Nov 27, 1979), data on file, USV Laboratories.

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ASOCIACION MEDICA DE PUERTORICO

I N D I C E

MAYO 1980

VOLUMEN 72
NUMERO 5

- * Cardiac Pacemakers, Retained Pacemaker Fragment and Infection -
Report of a Case in a Patient with a Superior Vena Cava Syndrome 218
*Charles D. Johnson, MD, FACC, and Enrique
Marquez, MD, FACS*

Johnson and Marquez report a patient who received a permanent endocardial pacemaker electrode for complete heart block. Subsequently, he developed a skin erosion over the pulse generator which became infected. Since the endocardial electrode catheter could not be removed due to its tight fixation to the right ventricular apical endocardial surface, it was cut and allowed to retract into the superior vena cava. Subsequently, he developed recurrent septicemia and thrombosis of the superior vena cava. This is a very interesting case presentation and management that should be carefully read by all physician who medically follow patients with permanent pacemakers. The discussion, although lengthy, is pertinent and complete. In our experience with over 75 patients at the Veterans Hospital, followed for over 10 years, we have not seen this complication.

- * Ventilation/Perfusion Scintiphotography in Pulmonary Diseases 228
Jaime Rivera Martínez, MD and Julio V. Rivera, MD

In this article Rivera-Martínez and Rivera present their experience and observations in 83 patients referred for ventilation perfusion scans in a 12 month period. The authors review the four basic patterns of V/Q (ventilation/perfusion) radionuclide studies and correlate the final clinical diagnosis of the patients studied with the type of ventilation-perfusion scan obtained. According to their observations, in 92 percent of the cases studied, the ventilation/perfusion scan was helpful in establishing the diagnosis. The authors propose that in suspected cases of pulmonary embolism, the diagnostic studies ordered should be blood gases and a perfusion scan. If abnormal, a ventilation study is indicated. If the diagnosis is still uncertain, a pulmonary angiography should be considered.

- * Two-Cases of Beckwith-Wiedemann Syndrome, One with
Hemihypertrophy 238
*Diego Bravo Velázquez, MD, María A. Toro Solá, MD, Aurea
I. Muñoz, MD and Víctor Montes-Jordán, MD*

The authors report what appears to be the first documented cases of Beckwith-Wiedemann syndrome in Puerto Rico. The recognition of the clinical signs and symptoms are crucial for the diagnosis of this condition. Macroglossia, abdominal masses and hypoglycemia are present in most of the cases reported in the literature. In patients with the syndrome there is an increased risk of malignant lesions detected during childhood, the most frequent being ganglioneuroma, adrenal carcinoma, hepatoblastoma and Wilm's tumor.

* Variations in Dose and Time of Collagenase Digestion for Maximal Islet Cell Separation for Transplantation	243
<i>Luis H. Toledo Pereyra, MD, PhD</i>	

The author present their findings on the ideal amount and time of collagenase digestion required for islet cell separation prior to transplantation in the rat portal vein. Although this study is highly technical, it shows the difficulties encountered in organ transplantation. At a time when renal transplantation is being performed more frequently in our medical center, this communication should made us aware of the potential benefits of islet cell transplantation.

* Sexually Transmitted Diseases - Part I - Gonococcal Infections	251
<i>Carlos H. Ramírez Ronda, MD, Guillermo Vázquez, MD</i>	
<i>Ramón H. Bermúdez, MD and Paul Harrington, MD</i>	

Of the sexually transmitted diseases, gonorrhea is probably one of the most intensively studied. In this issue Ramírez Ronda et al present not only the clinical features of gonorrheal infections, but also recent advancements in understanding its pathogenetic mechanism. In virulent gonococcal colonies, pili have been found extending from the surface of the bacterial cell. These gonococcal colonies can be serotyped by antigenic analysis of the pilus protein. It has been observed that these structures (pili) serve as the initial site of attachment of the gonococcus to the microvilli of the epithelial cells in the urethra.

Disseminated gonococcal infections (DGI) present peculiar clinical features. Gonococci producing DGI have been found to be distinctive. Episodes of DGI occur in females after the menstrual period and it has been postulated that menstruation predisposes to gonococcal blood stream invasion. These and other interesting facts are well explained in the article with special emphasis on its clinical applications.

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Health and Safety Tip

From the American Medical Association

535 North Dearborn Street/Chicago, Illinois 60610

High Blood Pressure Affects Many Adults

Combat Big Killer

An estimated 23 million Americans — 20 per cent of the adult population — have high blood pressure. Only about half of these individuals know they have high blood pressure, and only a minority of those who do know are being treated effectively.

Why do so many of us ignore this serious health hazard? Everyone knows that high blood pressure is bad for our health. Why don't we have blood pressure checked regularly? Why don't we begin treatment when the blood pressure is too high?

Because high blood pressure is a silent disease. Unless you have seen a doctor, you don't know you have it. And, even after you find out, it doesn't hurt. So why bother?

High blood pressure is one of the great killers. It can shorten your life by contributing to failure of your heart, arteries, kidneys and brain, the American Medical Association declares.

A nationwide screening effort has been underway for

several years in America to locate those persons with high blood pressure and get them started on treatment. High blood pressure can be controlled. And the result is a greatly lowered risk of serious disease and death.

Don't panic about your blood pressure, but protect your health and your life by keeping in mind five facts —

1. High blood pressure is a silent disease; it almost never has symptoms and a person does not feel sick.

2. It is a major cause of stroke, heart failure and kidney failure, but these disorders often can be prevented with control of high blood pressure.

3. It can be controlled by taking medications prescribed by your physician and by following his advice about life style.

4. High blood pressure medication should be taken every day, even if the patient feels well.

5. All adults, every one of us, should have blood pressure checked regularly.

It cannot be overemphasized that high blood pressure will not be cured, it will only be controlled. Thus it is vital to continue the therapy prescribed by the physician even after the blood pressure level has been lowered sufficiently. Abandon treatment and the pressure climbs again.



January, 1980
Frank Chappell
Science News Editor
AMA

CARDIAC PACEMAKERS, RETAINED PACEMAKER FRAGMENT AND INFECTION - REPORT OF A CASE IN A PATIENT WITH A SUPERIOR VENA CAVA SYNDROME

Charles D. Johnson, MD, FACC and Enrique Márquez, MD, FACS

Summary: We have reported on a patient with a retained pacemaker electrode fragment associated with recurrent staphylococcal septicemia and a superior vena cava syndrome. The experience, complications and management of this vexing problem have been reviewed.

Resumen: Informamos un caso de un fragmento de electrodo endocárdico de marca-paso retenido causando endocarditis bacteriana y síndrome de cava superior. Se revisa la experiencia, complicaciones y el manejo de este complejo problema.

Cardiac pacemakers have enjoyed widespread general acceptance, as insertion of a pacemaker is a very frequently performed cardiac operation with an even anticipated future of increased employability. However, a number of associated complications continue to be observed, one of the most catastrophic but fortunately uncommon, is infection.

Case Report

This 75-year-old man with chronic heart block received a permanent endocardial pacemaker electrode and subcutaneous generator in the right pectoral area in 1968. He underwent several replacements of the pulse generator over the years for battery exhaustion. In February 1978 it was noticed that the unit had extruded through the skin. An attempt was made to salvage the system by culturing and cleaning the wound, and by the instillation of local antibiotics into the pocket for three days. This failed, thus it was decided to remove the unit and electrode and to replace it with an epicardial system. However, the endocardial electrode could not be extracted, due to its very tight fixation to the right ventricular (RV) apex, and so, it was cut during traction and the distal end allowed to retract into the superior vena cava (SVC). Systemic antibiotics were used pre, post and intraoperatively.

The patient recovered and was discharged in March 1978, but was readmitted in March, April and May with fever, malaise and positive blood cultures for *Staphylococcus epidermidis*. He responded immediately to methicillin, 2g IV q. 4 h x 3 weeks plus probenecid, 0.5 g q. 6 h. He did well on oxacillin, 1 g p.o. q. 6 h, until October when he was admitted to University District Hospital because of fever, chills, dyspnea, cough and eyelid swelling. There were a few basilar rales, an enlarged prostate gland, no cardiac murmur, petechiae or splenomegaly, but cyanosis and edema of the face, and edema and collateral circulation over the upper chest were present. The leukocyte count was 17,200; the urinalysis revealed bacteria cultured as *Klebsiella*; *Staphylococcus aureus* was cultured from the blood; an electrocardiogram

From the Departments of Cardiovascular Surgery, and Medicine, University of Puerto Rico, School of Medicine, Río Piedras, P. R. 00936.



Figure 1: A chest roentgenogram and esophagram showing the electrode fragment in the right heart and superior vena cava (retouched), and the epicardial electrode system. A tortuous bizarre esophageal deformity is seen.

showed an epicardial left ventricular pacemaker (one tracing showed briefly sinus tachycardia, right bundle branch block and left anterior hemiblock); a chest roentgenogram and esophagram (figure 1) showed two sets of electrodes (including the retained fragment in the right heart), and a tortuous bizarre esophageal deformity. He received a six-week course of antibiotics, including oxacillin, tobramycin and nafcillin, Furosemide. He became afebrile and asymptomatic, but infection recurred 4 days later. Therapy consisted of mandelamine, ascorbic acid, naf-

cillin, amikacin and oxacillin. Bilateral forearm venous injections revealed obstruction of both subclavian veins with collateralization and filling of intercostal veins on both sides; the right was obstructed at the junction between the axillary and subclavian veins; unfortunately, no visualization of the SVC or right atrium (RA) was obtained.

Later, after becoming asymptomatic, an operation was done on Jan. 9, 1979, via a midsternotomy. There was considerable bleeding due to venous hypertension secondary to SVC obstruction. Under a cardiopulmo-

nary bypass the RA was opened and the cavity was cleared of thrombi attached at the entrance of the SVC; a total of 5 grams of tissue was removed. The electrode was densely attached to the leaflet of the tricuspid valve and was freed by incising the scar tissue over it. The SVC was thrombosed and could not be opened. The postoperative course was uneventful; there was no murmur of tricuspid insufficiency (TI); he was maintained on cloxacillin. At follow-up 6 weeks after surgery, the patient was ambulatory and afebrile and there was minimal evidence of SVC obstruction.

Discussion

Infection complicates cardiac pacemakers, either permanent or temporary, in 0-23 percent of cases, perhaps averaging 4-5 percent. This presents a most difficult management problem that is potentially lethal (up to 50 percent or more mortality) when it manifests itself as septicemia (0.2-6.6 percent) associated with endocardial pacemakers or retained fragments of pacemakers. By 1971, 21 cases of septicemia had been reported (1-15).

Other complications of cardiac pacemakers are component failure (battery depletion), cardiac arrhythmias, muscular stimulation, skin erosion (and extrusion) over the generator, hematoma, fluid leakage, damage and avulsion of the tricuspid valve producing TI, perforation of the RV, electrode displacement (6 percent), twisting and fracture with fragment migration to the venae cavae, iliac veins or even to the lungs. Electrodes may serve as a source of endocardial - RA, tricuspid valve and RV-mural septic thrombi or vegetations releasing septic pulmonary emboli and feeding systemic septicemia. Obstruction of the vena cavae and the tricuspid valve and even thrombosis of the subclavian and jugular veins have resulted from electrodes or cut resi-

dual fragments, although otherwise retained electrodes may not cause significant changes in cardiac function (2-4, 14-24). Fixed retained electrode fragments have resulted from the practice of pulling the electrode up tight, cutting it at the vein entrance and suturing the stump to the surrounding tissues (14, 15, 17, 25-28). This does not always prevent displacement (18).

Pathogenesis

Infection is of two main types: local at the generator site occurring in up to 23 percent of cases, and systemic manifesting as bacteremia which may actually represent endocarditis (as many as 60 percent of patients with staphylococcal bacteremia are stated to have infectious endocarditis and any sustained bacteremia should be regarded as such). There are two syndromes of endocarditis related to transvenous pacemakers: a) a foreign body syndrome secondary to local generator infection, presumably acquired during implantation, from skin erosion over the generator or lead, or from the site of venous entry and propagated directly along the lead eventually causing intracardiac infection. This is the more common type, occurs early and usually is due to staphylococci; b) metastatic implantation from a remote bacteremia associated with a decubitus ulcer, transurethral resection or systemic disease. Diverse organisms are usually found including *Pseudomonas*. This may arise from electrode-traumatized or abraded endocardium or from no known focus of infection, and occurs later (33 weeks). Vegetations locate on the catheter tip and along the catheter as mural endocarditis at the RA, SVC and tricuspid

valve. A thin fibrin layer forms around the catheter within 12 hours, and sterile vegetations serve as a susceptible focus in the presence of a transient bacteremia. Foreign bodies lower the number of bacteria required to produce infection (1, 3, 14, 15, 29, 30).

Diagnosis

Organisms may be recovered from the subcutaneous pocket, the blood and the electrode. A range of 5 days to 2 1/2 years has been observed between implantation and infection (37 days and gram positive organisms with permanent pacemakers, 5.7 days and gram negative organisms with temporary pacemakers). Recurrent or persistent fever, chills, anorexia, weight loss, petechiae, leukocytosis, cellulitis, signs of local infection or septic shock (although the classic findings of endocarditis may be infrequent) demand culture of the local area and the blood. It is important to verify the pacer as the source of any fever (rather than another etiology). A TI murmur may be present. Echocardiography can show thickening of the tricuspid leaflets and a RA thrombus. A venous angiogram or a superior venacavogram is part of the work-up for a SVC syndrome (1-3, 5, 6, 15, 23-26, 29, 31-33).

Prevention

Preventive measures include aseptic technique at implantation, battery replacement or revision of the pocket, perhaps performed in an operating room rather than a catheterization laboratory and trying to avoid repeated pacemaker changes and revisions which augment the risk of infection. The use of a cephalic vein and a deep, medial chest wall pocket

for the generator, gentle tissue handling, avoidance of tension, meticulous hemostasis and closure of the chest in two layers are important technical points (7, 13-15, 17, 25, 34-41). Some studies seem to show less infections with epicardial than with transvenous pacing (14, 42-45).

Some physicians prescribe prophylactic antibiotics pre and postoperatively at the time of insertion, although there is little evidence for any benefit (9, 13, 15, 36-38, 46-50). Smyth irrigates the pocket with neomycin solution (39). The prophylactic application of antibiotics during procedures likely to cause bacteremia such as dental and genitourinary procedures is presently controversial as to effectiveness (1, 2, 6, 21, 32, 37, 38, 51). An AMA Committee states that the risk is low but that one may choose to use prophylactic antibiotics to cover dental and surgical procedures (52).

Management

Local infection limited to the generator pocket or electrode should be treated early by drainage, closed irrigation with antibiotic solutions, debridement, local and probably systemic (oral, IV) antibiotics. These possibly negate removal of the pacemaker (, 2, 3, 12, 14, 15, 31, 34, 41, 47-51, 53-56). Smyth recommends these measures and for erosions he would rotate a skin flap to cover the exposed generator. If the pacemaker is bipolar, the patient elderly and a poor risk, the generator may be exteriorized and supported with a fabric sling dressing around the electrode (39, 47, 57). However, conservative measures may not control infections (wound breakdown), avoid septicemia or death (7, 15, 31, 34, 53).

If bacteremia and endocarditis occur, are uncontrolled or relapse, most authorities would consider urgent removal of the entire unit in-

cluding the electrode mandatory with appropriate parenteral antibiotics for 6 weeks to obtain control and cure (1-3, 5, 7, 8-11, 14, 15, 18, 23, 25, 26, 31, 34, 35, 38, 51, 57-61). Removal of the unit may be necessary even for cure of local sepsis (3, 31, 34, 62), although this may not always apply as there have been a few survivals or cures in the presence of positive blood cultures when the above approach was not adhered to (antibiotics alone, or only the wire removed) (3, 7, 12, 15, 48, 55, 63). Furman believes that these "scattered successes" are not successes in that the patients are left with a draining sinus or have had inadequate follow-up (31).

In the absence of infection and if the electrode is fixed, many authorities would leave it "in-situ", even for years, and insert a new electrode to avoid traction damage (3, 15, 18, 19, 27, 31, 35, 48, 53, 63-65). Other authors recommend removal of catheters not in use to avoid future sepsis, migration or embolism (2, 4, 16, 17, 20-22, 66). It has been customary to remove the entire infected pacemaker, use a temporary transvenous pacemaker until the wound is healed and the infection controlled, and then reimplant a new permanent unit and electrode at a different site on the other side of chest a few weeks later, or an epicardial electrode may be chosen instead (1, 5, 7, 14, 15, 23, 25, 29, 31, 35, 40-45, 47, 48, 51, 53, 54, 57, 59-61).

Late removal of a chronically implanted electrode may be dangerous, difficult or impossible. The electrode becomes adherent or incarcerated to the RV (into myocardium), tricuspid valve, RA and SVC from endothe- lization, fibrous sheath formation and even partial calcification. Incorporation into the RV may occur within 5 days and a proteinaceous, fibrous film forms within 2 - 3 1/2

weeks (19, 20, 30, 61, 64, 67, 68). Although electrode entrapment is infrequent (9 percent or less) it can present serious management problems; 6 of 11 cases in one study were complicated by infection (14, 15, 69).

Careful steady manual traction on the electrode may be tried initially, until cardiac pulsations are felt (28). However, heavy vigorous or sudden traction can induce bradycardia, atrial fibrillation, ventricular tachycardia, hypotension, electrode fracture, damage to the SVC, invagination and inversion of the RV wall (seen fluoroscopically), tearing of the RV, hemopericardium and tamponade and removal of trabeculae carneae (10 x 7 x 3 mm piece) (1, 16, 19, 20, 29, 34, 61, 64, 67, 70). Gentle steady traction employing Buck's orthopedic pulley with a weight of 1/5-1/2 lb for several hours to just below the level that produces premature ventricular contractions, aids in safe loosening and extraction (28, 31, 34, 61, 64, 67). Bilgutay reported success in a few minutes with this method applying sustained traction to the end of the wire with a cord and 1/2 - 2 pound weights suspended over a pulley, for 5-10 minute periods with electrocardiographic monitoring. In Lee's case after 11 hours and with 3 lbs of weight, sudden release ensued; no arrhythmias or hemodynamic changes occurred and the patient survived. This method too may result in extraction of pieces of myocardium (2 x 3 cm), trabeculae carneae, valve tissue and chordae tendineae (29, 59).

In view of the above possible complications and failure of Bilgutay's short term method, Imperato & Kim (71) recommend prolonged graded skin traction. The wound is opened widely and packed; digital traction (5 inches or more) is applied until rhythmic tugging is appreciated; it is then taped to the skin of the shoulder, the site being changed. The proce-

ture is repeated once or twice daily, obtaining a chest roentgenogram every 2 days. Success may require as long as 13 days, but there were no complications noted. The authors believed that this method succeeded by producing ischemia of the fibrous bands entrapping the electrode, causing necrosis and rupture without tearing the heart or major veins.

Nondislodging electrode tips such as irregular gripping, grasping, silicone rubber tines, flange, nylon hook, porous tip, etc., as available on modern electrodes may avoid unwanted dislocation, while making extraction more difficult or impossible. The Vitatron MIP 2000 electrode has 4 nylon wires which are retracted from the tip to remove the electrode, while the Vitatron Helifix with a helically coiled tip can be twisted into the trabeculae, and can be removed by an untwisting action (Vitatron Medical, Inc., Newton, MA). Perhaps medical grade nonthrombogenic silicone rubber catheter material such as polyurethane-coated woven polyester fabric (provoking little reaction), tip fixation only electrodes with a small tip, small light round generators and the new lithium generators of greater longevity may help solve the problems of catheter entrapment and infection (27, 34, 40, 41, 59, 60, 64). Various snares and endoscopic forceps have been useful to extract intravascular and intracardiac foreign bodies, although these have the potential of dislodgement of mural thrombus, pulmonary emboli or avulsion of the tricuspid valve (16, 35, 66, 72).

An alternative approach to the infected retained pacemaker catheter is the long-term oral or intensive parenteral administration of one or more antibiotics, an approach that has been successful in a few instances. The predominant organisms have been *Staphylococcus aureus* and *epidermidis* (account for more than 70 percent), and occasionally *Pseudomonas*

aerogenas, *E. coli*, *Proteus*, *Klebsiella*, *Flavobacterium*, *Serratia* and *Candida*. Methicillin, oxacillin, nafcillin, dicloxacillin, carbenicillin, penicillin, cephalothin, cephalexin, lincomycin, chloramphenicol, kanamycin, vancomycin, streptomycin, gentamicin and tobramycin have been used; penicillinase resistant penicillins are recommended until culture and sensitivity data are available. If endocarditis is suspected, antibiotics are administered for 4-6 weeks (2, 9, 12, 15, 31, 34, 49, 55, 63, 73, 74).

If traction methods and antibiotics fail (few successes with conservative therapy) (15, 31), then thoracotomy and traction and probably open cardiectomy (right ventriculotomy or right atriotomy) under cardiopulmonary bypass and administration of antibiotics are mandatory for septicemia. These may be performed safely with cure, after doing a venous angiogram. Complete removal is necessary. The electrode is cut-out with a sharp dissection of its position from the RV apex, septum and attachments to the tricuspid valve, SVC and subclavian vein. Any vegetations are removed. The papillary muscle may have to be repaired and the tricuspid valve replaced. The heart is then irrigated with an antibiotic and antibiotics administered postoperatively (1, 5, 15, 16, 26, 29, 34, 35, 57).

If an infected (local or systemic) lead system is epicardial it too must be treated similarly and removed (exteriorization of generator, placement of endocardial unit). This may be accomplished by progressive traction on the externalized leads (tension against skin, safety pin) for 21 days to 2.5 months. However, formal thoracotomy is almost always necessary where the lifted detached electrode heads lying in a granulomatous mass can be transected from the leads and all removed (31, 75).

Thrombosis of innominate, subclavian,

axillary and humeral veins may cause venous collateral circulation, edema of the arm and even a cold cyanotic arm. However, venous abnormalities such as early and late thrombophlebitis and obstruction of the axillary, subclavian, innominate and SVC venous system are often asymptomatic, occult, benign and commoner than previously appreciated with permanent pacemakers (30 percent of studied patients had abnormal venograms) (9, 14, 22, 24, 31, 76-78). Symptomatic SVC syndromes appear rarely, these authors being aware of only 11 cases (14, 23, 79-83). A patient with fever (no infection) and chest pain died from pulmonary emboli secondary to thrombosis in the SVC around a pacemaker electrode (79). Wertheimer et al (80) reported in 1973 a SVC syndrome as a complication of a residual IV electrode with thrombosis and occlusion of the right innominate vein (venogram) without blood stream infection. Torresami et al (14) observed SVC thrombosis and edema in one patient in 800 implantations. Another patient with innominate and SVC thrombosis (venocavogram), but no infection, presented with swelling of the face, neck, arm and pectoral region (81). Williams & Demos' (23) patient with a SVC syndrome (retained electrode) shown by cavogram, had been treated 10 months prior for a gram positive septicemia secondary to an infected pacemaker. They also treated another fatal case with gram positive septicemia. Thromboemboli were present in these patients as well as in 6 cases found from the previous literature. Thrombi may compromise venous return to the right heart, and may contribute to thrombosis of cerebral dural venous sinuses, congestive heart failure and a high mortality. Branson (82) described the radiology of 3 cases of SVC obstruction.

Chamorro et al (83) added two further

cases of SVC obstruction developing 5 weeks and 4 years after pacer implantation, thrombi in proximity to the electrode being shown on cavography. They emphasized the causative thrombogenic roles of surgical technique, alterations in the interior vessel wall and cell potential, surface charge and incompatibility, and electrode surface characteristics, factors now under investigation.

Patients rarely require surgery for thrombosis but have responded and recovered by elevating and wrapping the arm in an elastic bandage, administration of a diuretic, heparin long term sodium warfarin and streptokinase (lysis of clot) as recanalization, resolution and venous collaterals develop (14, 22, 23, 31, 76, 77, 80, 81, 83). Thrombus may affect surgical management calling for a preliminary venogram, if a catheter requires removal and replacement through the same venous system. Late thrombophlebitis may be secondary to a cause not related to the pacemaker such as occult malignancy (31, 78).

Our patient suffered both pacemaker associated recurrent septicemia and the rare complication of a pacemaker-induced SVC syndrome, which manifested clinically, on venous angiography and was later confirmed at surgery. He may be the third patient documented to suffer both these complications (23).

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VENTILATION/PERFUSION SCINTIPHOTOGRAPHY IN PULMONARY DISEASES

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Summary: We are reporting on the results of ventilation/perfusion scans in the evaluation of pulmonary diseases. The patient population included 83 cases with different suspected pulmonary disease entities who were referred for ventilation/perfusion scanning. Their final clinical diagnosis and other diagnostic modalities, including chest x-ray, hemoglobin, pulmonary function test, arterial blood gases and arteriography were correlated with the ventilation/perfusion scan.

In 92 percent of the cases studied, the ventilation/perfusion scan was helpful to the clinician in establishing the final diagnosis. In the other 8 percent, the diagnosis was based on clinical grounds only, obviating the ventilation/perfusion scan results and without going into other invasive diagnostic procedures like arteriogram for the final diagnosis.

It is concluded that ventilation/perfusion scan is helpful to the clinician in establishing the final diagnosis of patients with different pulmonary diseases and should be used routinely in Puerto Rico. This study is valuable in the selection of patients for pulmonary angiography.

Resumen: Se informa los resultados de un estudio retrospectivo basado en 83 casos referidos para estudios de ventilación-perfusión con materiales radiactivos para la evaluación de diferentes enfermedades pulmonares. Se correlaciona los estudios de ventilación/perfusión con la clínica y con otros estudios y pruebas diagnósticas. En un 92 por ciento de los casos estudiados el estudio de ventilación-perfusión fue de ayuda al clínico en la evaluación y tratamiento. En el 8 por ciento restante, el diagnóstico se hizo en bases clínicas únicamente, obviando el patrón de ventilación-perfusión y sin acudir a otros métodos diagnósticos invasivos tales como la arteriografía para el diagnóstico final.

Se concluye que el estudio de ventilación-perfusión con materiales radiactivos es de mucha utilidad al clínico y debe ser un estudio de rutina en el manejo de pacientes en Puerto Rico. Este estudio es además útil en la selección de pacientes para estudio angiográfico pulmonar.

The use of ventilation/perfusion (V/Q) scintiphotography in the evaluation of different pulmonary diseases was introduced in 1970 (1). Its accuracy and utility has been established in the literature (2, 3).

The perfusion (Q) lung scan correlates with the regional distribution of pulmonary arterial blood flow. Particles of about 10-50

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TABLE I
Major Patterns of \dot{V}/\dot{Q}

	Pattern	Diseases	Patterns Found
Normal	\dot{V}_n/\dot{Q}_n *	Non-pulmonary	13
Vascular	$\dot{V}_n/\dot{Q} \downarrow$ +	Congenital Pulmonary artery agenesis	
		Acquired Pulmonary embolism Vasculitis	17
	Gradient Inversion	CHF or Pulmonary Hypertension	10
Parenchymal	$\dot{V} \downarrow / \dot{Q} \downarrow$	COPD, Pulmonary Fibrosis, Pneumonia, Cyst, Neoplasm	54
Mixed	----	----	13

* n = normal+ \downarrow = decreased

microns are injected intravenously and are trapped temporarily in the arteriolo-capillary bed. The ventilation (V) lung scan is done with radioactive gases and reflects regional ventilation.

Four basic patterns of V/Q radionuclide studies have been described (4) (Tab 1): 1. Normal pattern demonstrating no defects in ventilation or perfusion; 2. *Normal ventilation coinciding with abnormal perfusion*, associated with *pulmonary vascular disease*; 3. A pattern showing both abnormal ventilation

and perfusion coinciding in the same area, associated with *pulmonary parenchymal disease*; 4. A pattern showing a combination of 2 and 3 in the same study, that is, a mixed type.

V/Q scans have been performed routinely in the Veterans Administration Hospital, San Juan, Puerto Rico since September 1977. It is the purpose of this report to share our experience, to compare our findings to those described in the literature and to evaluate the effect of the V/Q scan in the diagnosis

NORMAL

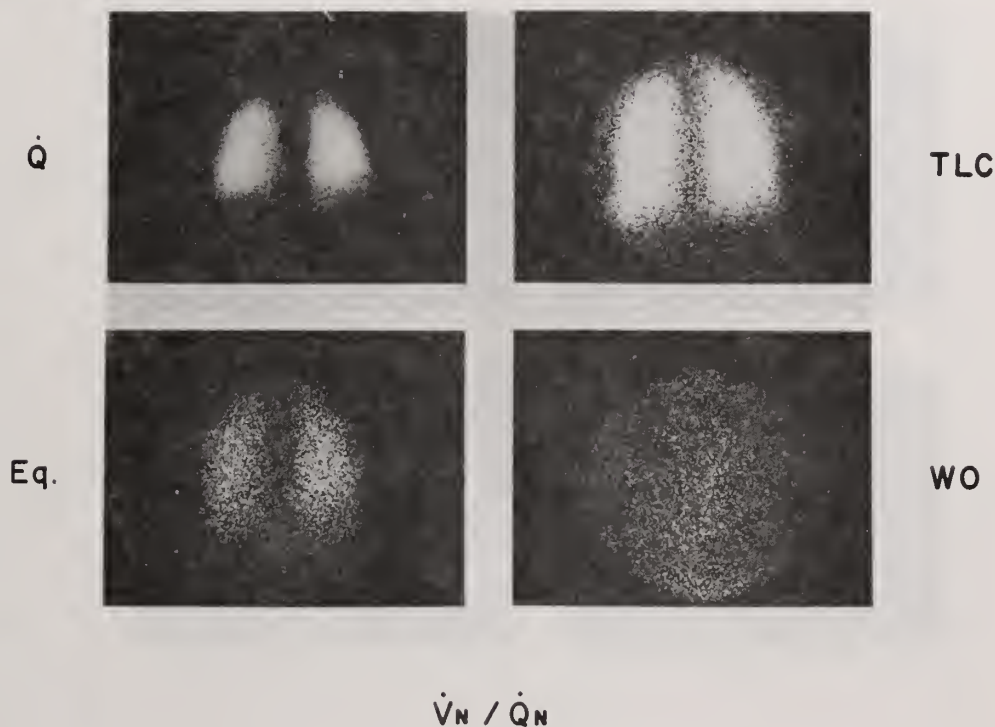


Fig. 1: Normal. Posterior perfusion (upper left), ventilation at total lung capacity (upper right) and equilibrium (lower left), scintiphotos demonstrate homogeneous distribution of activity. Posterior view during washout (lower right) discloses complete clearance of activity.

and management of patients with different pulmonary diseases.

Material and Method

This retrospective study was designed to study all cases referred to our clinic for a V/Q scan from September 1977 to October 1978. All laboratory results, x-ray studies, v/Q scan, pulmonary function studies, and final diagnosis were exclusively obtained as reported in patients' records. Nine cases with incomplete records and 85 cases, in which only a perfusion scan was performed, were excluded from the

study. In total, 83 cases are included, and the findings form the basis of this report.

A scintillation camera (Nuclear-Chicago, Des Plaines, IL) with a 140 KeV diverging collimator was used in all studies. The perfusion study was done after an intravenous injection of 3-5 mCi of ^{99m}Tc magro-aggregated albumin (Mallinckrodt, Inc., San Juan, PR) in the sitting position. For the ventilation radionuclide study, the patient was usually seated in front of the camera with the posterior aspect of the chest in contact with the collimator face while breathing through a closed spirometer system (RADX Corp., Houston, TX). After a short period of adaptation to the system, 10 mCi of $^{133}\text{Xenon}$ were injected with the patient holding his breath at functional residual capa-

PULMONARY EMBOLISM

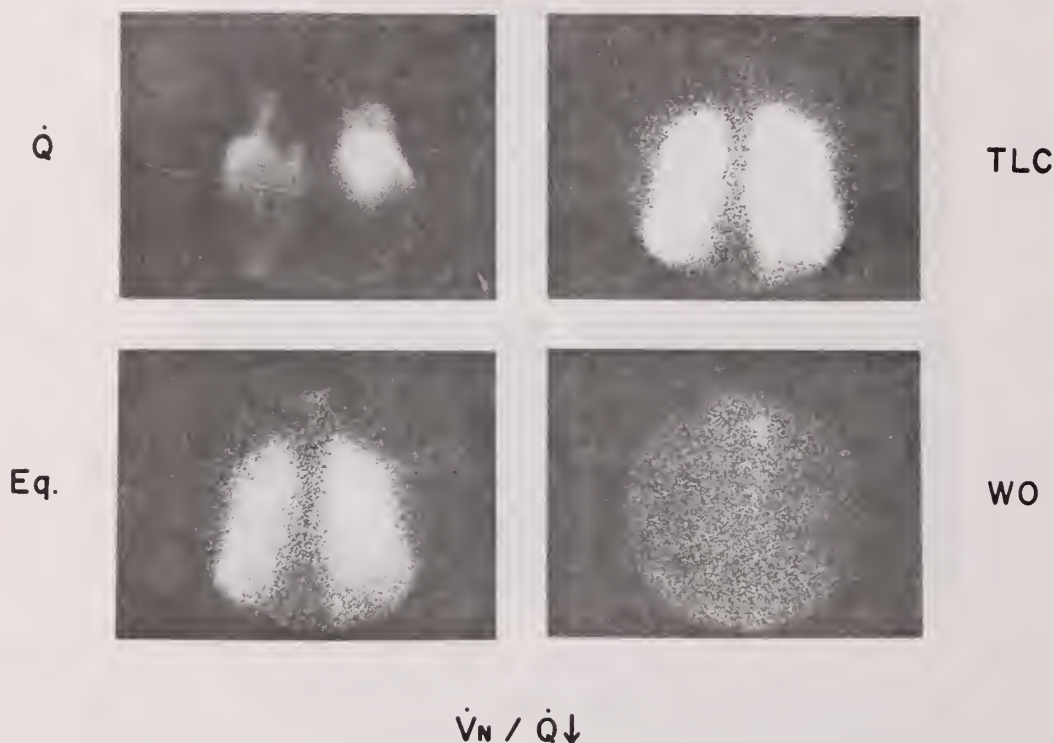


Fig. 2: Pulmonary embolism. Posterior perfusion scintiphotograph shows multiple bilateral segmental and subsegmental defects. Posterior ventilation scintiphotograph shows homogeneous distribution of activity at total lung capacity (upper right) and equilibrium (lower left). After washout (lower right) the radioactive tracer has completely cleared.

city. The patient then inspired to total lung capacity and the scintiphotograph was taken during 10-30 seconds while the patient held his breath. Scintiphotos were then obtained during equilibrium and washout phases. Equilibrium was established by rebreathing a mixture of oxygen and xenon into the spirometer during 3-5 minutes. Washout was obtained when the spirometer was opened, and the patient inhaled room air and exhaled the xenon into the collection system (xenon trap) for 3-10 minutes.

Each ventilation study took approximately 30 minutes to perform, from start to finish.

Results

Four V/Q patterns, as previously described in the literature, were identified (Table I).

In 13 cases, the V/Q scan was read as normal (Figure 1). In this group the final clinical diagnoses were angina pectoris, myocardial infarction, hiatal hernia, and other non-pulmonary diseases with the exception of one patient with bronchial asthma in remission.

TABLE II
Other Diagnostic Parameters in Respiratory Diseases
(Percent of Patients)

	g/dl			Chest X-Ray		mmHg				
	Hemoglobin			Neg	Pos	pO ₂		pCO ₂		
	< 12	12-16	> 16			< 80	> 80	< 35	35-45	> 45
Non pulmonary	0	76	24	75	25	58	42	46	54	---
Embolism	20	80	---	46	54	7	93	54	46	---
COPD	22	48	30	39	61	4	96	30	61	9
CHF	9	91	---	---	100	36	64	44	56	---

The pattern associated with pulmonary vascular disease was identified in 17 cases (Figure 2).

The pattern associated with pulmonary parenchymal disease was seen in 54 cases: 40 with chronic obstructive pulmonary disease (COPD); 4 with pulmonary fibrosis; 1 with bronchial asthma; 1 with pneumonitis; and 8 with carcinoma.

Ten cases with congestive heart failure (CHF) showed gradient inversion in the perfusion study. In three it was the only abnormality; 5 also demonstrated the pattern associated with pulmonary parenchymal disease, and in 2 it was associated with pulmonary vascular disease.

A mixed pattern was demonstrated in 13

cases: 6 with the patterns associated with parenchymal and vascular disease; 5 associated with parenchymal disease and gradient inversion; and 2 with vascular disease and gradient inversion.

Pulmonary function studies were performed in only 9 cases. They supported the diagnosis of parenchymal pulmonary disease found on V/Q scan.

Pulmonary arteriography was performed in only 4 cases in whom pulmonary embolism was suspected. In all 4 cases, it was performed due to lack of confidence in the V/Q scan by the clinician. In 3, the V/Q scan and the angiographic study were negative. In the fourth case the V/Q pattern was consistent with pulmonary embolism, but the angiographic study was read as negative. The final diagnosis by the

TABLE III
Effect of V/Q on Diagnosis

<i>Referral Diagnosis</i>	<i>No.</i>	<i>Confirmed By V/Q</i>	<i>Refuted by V/Q</i>	<i>Accepted by Clinician</i>	<i>Not Accepted by Clinician</i>
<i>Embolism</i>	<i>60</i>	<i>17</i>	<i>43</i>	<i>13</i>	<i>7</i>
<i>CHF</i>	<i>0</i>	<i>--</i>	<i>--</i>	<i>10</i>	<i>--</i>
<i>COPD</i>	<i>7</i>	<i>7</i>	<i>---</i>	<i>40</i>	<i>---</i>
<i>Pulmonary Fibrosis</i>	<i>4</i>	<i>4</i>	<i>---</i>	<i>4</i>	<i>---</i>
<i>Asthma</i>	<i>2</i>	<i>2</i>	<i>---</i>	<i>2</i>	<i>---</i>
<i>Pneumonitis</i>	<i>1</i>	<i>1</i>	<i>---</i>	<i>1</i>	<i>---</i>
<i>Carcinoma</i>	<i>8</i>	<i>8</i>	<i>---</i>	<i>8</i>	<i>---</i>
<i>Non pulmonary</i>	<i>1</i>	<i>1</i>	<i>---</i>	<i>12</i>	<i>---</i>

clinician was pulmonary embolism.

Other parameters studied such as hemoglobin, chest x-ray, pO₂, and pCO₂ turned out to be non-specific in the assessment of pulmonary disease (Table II).

The effect of the V/Q scan on the final diagnosis and management is summarized in Table III. Sixty patients were referred to us as possible cases of pulmonary embolism. Seventeen were confirmed and in 43 the study did not support the diagnosis. Of these 43 patients, 11 had non-pulmonary disease; 29 had chronic obstructive pulmonary disease; and 3 had congestive heart failure. In 76 of 83 cases studied, the V/Q scan helped to establish the

final clinical diagnosis. In the other 7 cases, the study was non-contributory since it was not accepted by the clinician in arriving at the final diagnosis. The V/Q scan favored pulmonary embolism in 4, and was against it in 3 cases. Arteriographic study was not performed, the final diagnosis of these 7 cases being based only on clinical grounds.

No morbidity and mortality, as a consequence of the V/Q scan, were observed in the 83 cases.

In all cases studied, the final clinical diagnosis was selected as the standard in evaluating the effectiveness of V/Q scan and other parameters. Therefore, conclusions were made

COPD

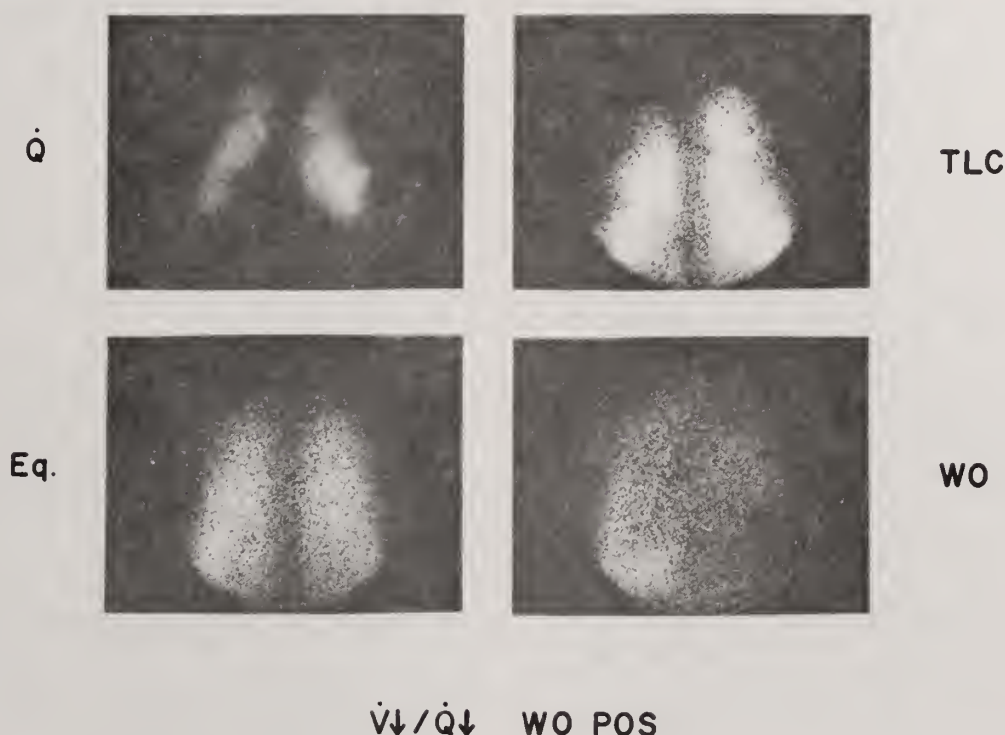


Fig. 3. Chronic obstructive pulmonary disease. Posterior perfusion scintiphoto (upper left) shows multiple subsegmental areas of decreased distribution bilaterally. Posterior ventilation scintiphotos at total lung capacity (upper right) and equilibrium (lower left) demonstrate multiple defects corresponding to the perfusion defects which disappears after rebreathing. Washout photo shows marked retention of activity in the regions of decreased perfusion.

assuming good clinical judgment in the interpretation of the clinical data obtained in each case. This represents a limitation particularly in the 60 patients in whom pulmonary embolism was suspected since pulmonary arteriography, the "gold standard" was only done in 4 cases. Nevertheless, the limitation is acceptable for the purpose of this study which is not designed to validate the accuracy of V/Q scan but its clinical effects in the routine clinical situation.

Discussion

The study presents our experience in evaluating different pulmonary diseases with V/Q scan and the impact of this diagnostic examination on the clinical outcome.

The perfusion scan has been accepted as the best screening examination for pulmonary embolism. *When negative, it essentially rules out pulmonary embolism (4, 5). As expected,*

the majority of our cases studied were referred as suspected cases of pulmonary embolism. Eighty-five patients not included in this study had normal perfusion scans and ventilation scans were not indicated. For those with positive perfusion studies, the addition of the ventilation study helped to clarify its etiology.

The V/Q pattern helps to differentiate pulmonary vascular disease from parenchymal disease in the majority of cases, avoiding unnecessary treatment with heparin and in the selection of patients for pulmonary arteriography, avoiding significant morbidity and mortality (6, 7).

Another parameter that appears to be of some help in the diagnosis of pulmonary embolism is the partial oxygen pressure. In our study, 93 percent of the cases had pO_2 below 80 mmHg. When dealing with patients with COPD, in whom pO_2 is below 80 mmHg in 96 percent of the cases, the parameter is non-specific in the diagnosis of pulmonary embolism.

As has been reported by others (8), the partial pressure of carbon dioxide proved to be of no diagnostic help. Chest x-rays were of limited use, except as adjuvants in the interpretation of V/Q scans and other studies.

In our study, 92 percent of the final diagnoses were made by utilizing the V/Q pattern, while 8 percent of the final diagnoses (all suspected cases of pulmonary embolism) were made on clinical grounds only obviating the results of the V/Q pattern and not resorting to arteriogram. We think that an arteriogram was indicated to reach a final diagnosis in these cases, particularly if we accept that a clinical diagnosis of pulmonary embolism carries a high incidence of error.

The V/Q scan is also helpful to the physician in the following ways: first, it helps in the selection of cases in which pulmonary

arteriography is justified; second, it provides localizing information to the angiographer, helping him emphasize the affected areas seen on the scan.

Disagreement between the V/Q scan and arteriogram, as in one of our cases, is not surprising considering that changes in the angiographic picture may occur in a period of a few days (9).

From the economic point of view, we know that prolonged hospitalization and unnecessary studies increase costs markedly. In order to demonstrate the effect of the V/Q scan in this regard, we quote the following average prices per diagnostic study in suspected cases of pulmonary embolism given by McNeil et al (10): chest radiography, \$25; perfusion lung scan, \$125; ventilation study, \$35; pulmonary angiography, \$300. Hypothetically, if a chest x-ray and pulmonary arteriography had been done in all 60 patients reported as possible cases of pulmonary embolism, it would have a cost of \$19,500 instead of \$10,610 if a chest x-ray and perfusion scan had been done on all patients and ventilation only on those showing perfusion abnormalities.

The utility of the V/Q scan in the diagnosis of other pulmonary diseases is well established. It may give additional information supplementing that obtained from other studies such as pulmonary function studies and radiographs. V/Q scans are reproducible and may be quantified. They identify regional abnormalities in a given disease, helping in the evaluation, follow up and surgical management if required. Positive findings were obtained in 55 of our cases.

In conclusion, in the majority of cases (92 percent) in our study, the ventilation-perfusion study turned out to be of help in establishing the final clinical diagnosis. In the evaluation of pulmonary diseases, ventilation-

perfusion studies are reliable, simple, safe and economical.

In suspected cases of pulmonary embolism, the first diagnostic study should be a perfusion scan. If abnormal, a ventilation study is indicated. If the diagnosis is still uncertain, then a pulmonary angiography should be ordered. This procedure is also indicated in patients in whom surgical procedures such as embolectomy and interruption of the inferior vena cava are being considered.

Our findings should encourage the establishment of more centers in Puerto Rico where ventilation-perfusion studies can be performed.

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MEDI-QUIZ - PARASITOLOGY I

ANSWERS

1. D Ref. 1, pp 465-470 - Eosinophila while present has been reported to be intermittent.
2. B Ref. 1, pp 458-460 - Infection with trichuris, involves penetration of the intestinal villi by the larval form.
3. E Ref. 1, pp 461-464 - Intestinal obstruction is not seen with *Enterobius*, it has been reported with ascariasis.
4. D Ref. 1, pp 534-538, Ref. 3- Usually a self-limited disease. Drethycarbamazine and mebendazole has been used in treatment.
5. C Ref. 1, pp 471-480, Ref. 4 - Mean life span of 5 years, recontamination with hatched larvae.
6. D Ref. 1, pp 471-480 - Eosinophile counts high during migration stages.
7. B Ref. 1, pp 543-568 - Eggs hatch in fresh water, miracidia invade the snail, forked tail cercariae and liberated. Cercariae penetrate human skin, pass through lung and liver and pass to final habitat in portal venous system.
8. A Ref. 1, pp 461-464 - Enterobiasis is not associated with significant eosinophilia.
9. B Ref. 1, pp 525-529- Porks fed with garbage if the garbage is uncooked, there is no use to incorporate thiabendazole.
10. A Ref. 1, pp 346-347 - Symptoms are of sudden onset with watery foul diarrhea, abdominal distention and nausea. Chronic infection is characterized by malabsorption not colitis. *Giardia* infects the small bowel.

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- Ref. 3: Aur, R. J. A. et al: *Thiabendazole in visceral larvae migrens*. *Am J. Dis. Child* 121: 226, 1971.
- Ref. 4: Barret Connor, E: *Am. J. Med.* 52: 242, 1972.
- Ref. 5: Charenia, A. P. et al: *Am. J. Trop. Med. Hyg.* 22: 592, 1973.



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DIRECTIONS FOR USE—ADULTS: Before breakfast and after the evening meal, one to two rounded teaspoonfuls of Perdiem™ granules should be placed in the mouth and swallowed with a full glass of warm or cold beverage. Perdiem™ granules should not be chewed. After Perdiem™ takes effect (usually after 24 hours, but possibly not before 36-48 hours), reduce the morning and evening doses to one rounded teaspoonful. Subsequent doses should be adjusted after adequate laxation is obtained.

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FOR PATIENTS HABITUATED TO STRONG PURGATIVES: Two rounded teaspoonfuls of Perdiem™ in the morning and evening may be required along with half the usual dose of the purgative being used. The purgative should be discontinued as soon as possible and the dosage of Perdiem™ granules reduced when and if bowel tone shows lessened laxative dependence.

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DURING PREGNANCY: Give one to two rounded teaspoonfuls each evening.

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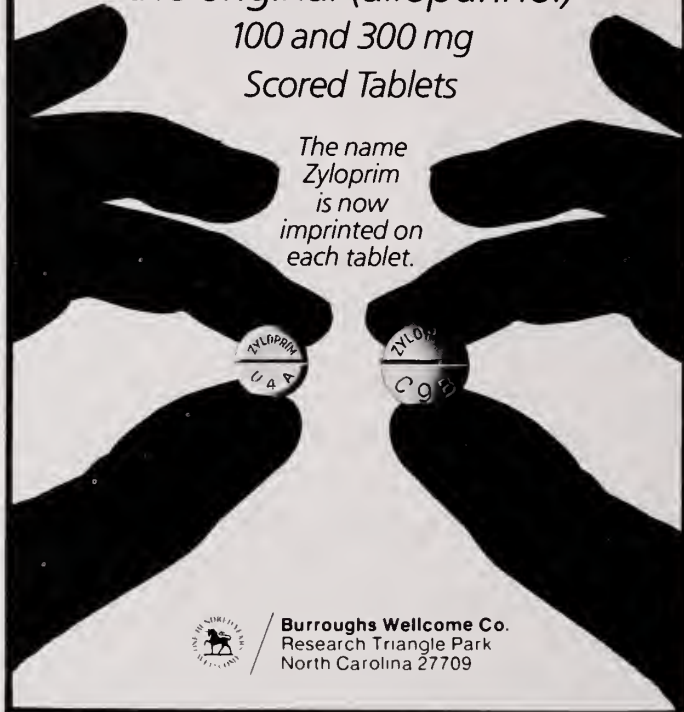
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TWO CASES OF BECKWITH-WIEDEMANN SYNDROME, ONE WITH HEMIHYPERTROPHY

Diego Bravo Velázquez, MD, María A. Toro-Solá, MD
Aurea I. Muñoz, MD and Víctor Montes-Jordán, MD

Summary: Two cases of the Beckwith-Wiedemann syndrome are herein reported. The clinical findings of the syndrome are discussed, emphasizing the syndrome as a diagnostic possibility in the neonate with abdominal masses, dysmorphic facial features and hypoglycemia. The early detection of malignancies must be a preventive approach in the care of these children. Careful analysis of the family history may disclose other cases for autosomal dominant Mendelian inheritance may be present.

Ever since Beckwith's (1) and Wiedemann's (2) description of the syndrome of visceral cytomegaly, omphalocele, macroglossia, neonatal hypoglycemia, mild microcephaly and postnatal gigantism, a significant number of cases have been reported. The frequency of the syndrome has been estimated in Jamaica as 1/13,700 live births (3). We herein describe the findings in two female infants. Until more subtle features of the syndrome were recognized, the presence of large kidneys was a diagnostic problem in Case 1. The diagnosis was

established in another infant born elsewhere (Case 2) and seen by us at age six months, by her clinical features and retrospective analysis of a turbulent neonatal history. To our knowledge, no Puerto Rican patients with this syndrome have been previously described.

Case Reports

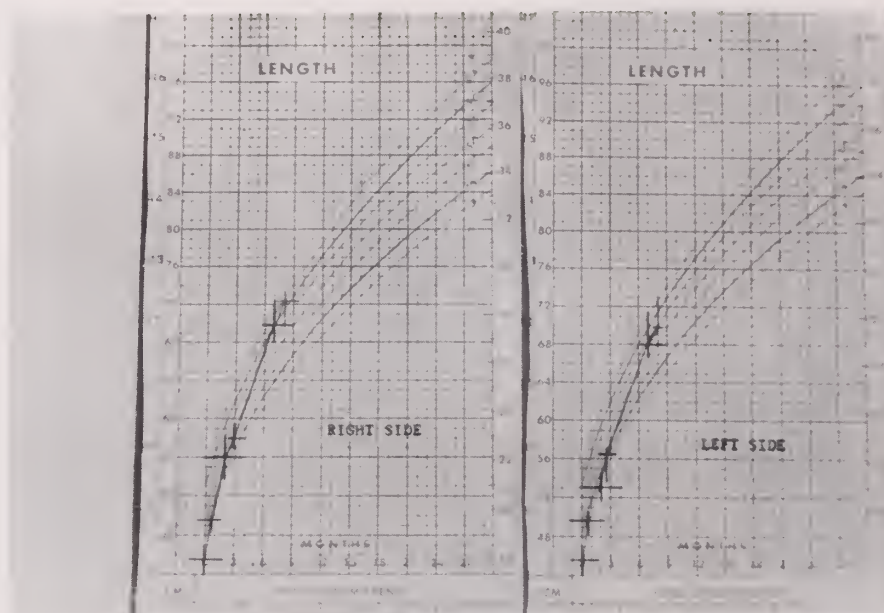
Case 1: J. R., a female infant born to nonconsanguineous parents after 36 weeks gestation, was delivered by Cesarean section because of transverse lie. Pregnancy was complicated by mild toxemia. The 43-year old mother had seven normal children and one abortion by a previous marriage. No similar cases were identified in this family. Birth weight was 2630 gm with Apgar Score of 7 (1 minute) and 8 (5 minutes), length 45.7 cm (below the third percentile *) and head circumference 30.5 cm (below 2 std deviations **). Other physical findings included a slightly prominent occiput, large protruding tongue, mild micrognathia, long philtrum, close posterior fontanel and a slit in the right ear lobe.

The abdomen was globulous with diastasis recti and a small umbilical hernia. Large, smooth masses were palpable in both flanks. She was noted hypo-

From the San Juan City Hospital, Puerto Rico Medical Center.

* - Percentiles charts, Boston Children's Hospital, Boston, Mass.

** - Head circumference charts, Research and Educational Hospitals, Chicago, Illinois.



active on her second day, with poor cry and sucking. Antibiotic therapy was given for suspected sepsis and she responded well. The blood glucose was 45 mg/dl with normal serum electrolytes and BUN. An intravenous pyelogram (IVP) showed large bilateral kidneys with normal excretion, but the renal contours were not well outlined. A renal image scan showed bilateral renal enlargement with even distribution of the radioactive tracer and a patent urachus. Abdominal ultrasonography confirmed the presence of abnormally large kidneys without evidence of cystic or solid lesions. The tail of the pancreas was seen enlarged, anterior to the left kidney. Throughout her nursery stay she grew very well, increasing 4 cm in length. She was discharged at one month of age. When re-examined at age 2 months, right hemihypertrophy was striking, the length of the right side of her body being 56 cm (25 percentile) compared to 53 cm on the left (3 percentile). There had been an upward shift in the percentile level bilaterally over a five-month interval (Figure 1). Asymmetry of the tongue was now

evident. Psychomotor development was normal. At age 7 months a repeated IVP was normal.

Case 2. M. A., a female born by spontaneous unsterile delivery at home to a 24-year old Gr3 P3 after 36 weeks gestation. Pregnancy was complicated by mild preeclampsia and first trimester bleeding treated with progestagens. The family history was also negative.

Thirty minutes after birth she was taken to the emergency room of another hospital in an asphyxiated state, requiring intubation. Weight was 2159 gm, length 48 cm. Blood sugar was 45 mg/dl. Hepatosplenomegaly, macroglossia, enlarged right kidney, large fontanels with open sutures, "amniotic umbilicus" and microcephaly were noted on initial examination. She became jaundiced (bilirubin 11.4 mg percent) and was treated with antibiotics. A T_4 was 8.8 mcg/dl (Normal values 4.7-10.7 mcg/dl) with a T_3 resin uptake of 57.9 percent (Normal values 55-59 percent). These studies were considered Normal. IVP disclosed enlarged kidneys. She was discharged at age 27 days



Fig. 2: Macroglossia and omphalocele still evident at age 6 months.

to be readmitted two weeks later hypotonic, bradycardic and in respiratory distress. Blood sugar was between 0 and 20 mg percent (Destrostix®). Intravenous glucose was given and because of vomiting and aspiration, the patient was intubated, remaining two days in a ventilator. During the hospital stay she needed tube feedings because of extreme macroglossia.

We examined the patient for the first time at age 6 months. Macroglossia was still prominent, the tongue was bifid, the mouth large with a thin upper lip and a long philtrum. The metopic fontanel was palpable and the anterior fontanel large. A mild pectus with inverted nipples as well as a small ompha-

locele (8 x 8.5 cm) were evident. Psychomotor development was slightly retarded (Figure 2).

Discussion

To the cardinal morphologic features of the Beckwith-Wiedemann syndrome additional characteristics have been added in subsequent reports. These include auricular lobe anomalies, facial nevus flammeus, long philtrum, mediofacial hypoplasia, polycythemia, hypocalcemia and diastasis recti. Polyhydra-

mnios and a large placenta have been noted. Less commonly described features include diaphragmatic defects, clitoromegaly, cryptorchidism, inguinal hernia and intestinal malrotation. Hemihypertrophy has been reported in approximately 17 percent of cases (4). Neonatal hypoglycemia secondary to hyperinsulinemia is clinically demonstrable in 50 to 75 percent of cases. This is the most frequent metabolic abnormality of the syndrome and symptomatic below 30 mg/dl. Pancreatic islet hyperplasia (nesidioblastosis) is the etiologic factor. Mental retardation has been observed with or without associated microcephaly and is probably secondary to undetected hypoglycemia. There is an increased risk of malignancy during childhood, such as ganglioneuroma, adrenal carcinoma, hepatoblastoma and Wilm's tumor. Juvenile fibroadenoma, an extremely rare tumor below age 10 has been recently described in a female infant with the syndrome (5).

The possibility of autosomal dominant inheritance has been suggested (6) (7). Thyroxine binding globulin deficiency (TBG) is a genetic trait inherited either as autosomal dominant or sex linked recessive. Two cases of its association with Beckwith-Wiedemann's syndrome are described (8).

Knowledge of the etiology of clinical signs present in the neonate with the suspected syndrome is crucial for the differential diagnosis. Macroglossia, a main dysmorphic feature, may be either familial, idiopathic muscular hypertrophy, or due to hamartomatous lesions (e. g. lymphangiomas, hemangiomas). Less likely congenital hypothyroidism presents extreme macroglossia at birth.

Abdominal masses in a neonate must be thoroughly investigated. Polycystic kidneys, bilateral renal vein thrombosis, Wilm's tumor, are among the main considerations.

In Case 1 initial diagnostic efforts were focused on the flank masses, before the significance of more subtle features, such as the protruding tongue, right ear lobe slit and small umbilical hernia became apparent. Definitive diagnosis was further delayed by the nonconclusive results of the intravenous pyelogram. The renal scintigram did show bilateral renal enlargement and a patent urachus, strengthening our suspicion of the syndrome. Finally, ultrasonography confirmed the presence of nephromegaly in the absence of cystic or solid lesions. Interestingly, the tail of the pancreas was also shown to be enlarged, though hypoglycemia was never clinically detected.

Intravenous pyelography proved to be the first tool for evaluating renal and extra-renal abdominal masses in the newborn (9) but with the advent of ultrasonography, we now have a better tool for diagnosis.

Both cases illustrate that Beckwith-Wiedemann syndrome is one of the diagnostic possibilities in a neonate with abdominal masses. Early diagnosis is important in order to recognize possible hypoglycemia. We feel that ultrasonography is a valuable adjuvant for the demonstration of visceromegaly in this condition, especially when the clinical picture is otherwise not clearcut, as in Case 1. The fact that Case 2 remained undiagnosed for several months, suggests that this syndrome may sometimes pose a diagnostic dilemma and that its frequency is possibly underestimated.

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300 mg
Scored
Tablets

For Sustaire prescribing information, including adverse reactions and contraindications, please see last page of this advertisement.

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Sustained Release

SUSTAIRE®

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theophylline(anhydrous)

A THEOPHYLLINE THAT WORKS ALL DAY...AND ALL NIGHT

PRESCRIBING INFORMATION

SUSTAIRE® theophylline (anhydrous) U.S.P. SUSTAINED RELEASE TABLETS

DESCRIPTION: SUSTAIRE Sustained Release Tablets contain not less than 94.0 percent and not more than 106.0 percent of the labeled amount of $C_7H_8N_4O_2$. Theophylline, a xanthine compound, is a white, odorless crystalline powder, having a bitter taste. SUSTAIRE contains anhydrous theophylline.

CLINICAL PHARMACOLOGY: Theophylline directly relaxes the smooth muscle of the bronchial airways and pulmonary blood vessels, thus acting mainly as a bronchodilator, diuretic, cardiac stimulant, cerebral stimulant and skeletal muscle stimulant. The actions of theophylline may be mediated through inhibition of phosphodiesterase and a resultant increase in intracellular cyclic AMP which could mediate smooth muscle relaxation. At concentrations higher than attained *in vivo*, theophylline also inhibits the release of histamine by mast cells.

SUSTAIRE has been specifically formulated, clinically tested, and shown to provide a therapeutically effective serum level when administered on a q12h dosage schedule. SUSTAIRE minimizes the peaks and valleys of serum levels commonly found with shorter-acting theophylline products.

In vitro, theophylline has been shown to react synergistically with beta agonists that increase intracellular cyclic AMP through the stimulation of adenyl cyclase (isoproterenol), but synergism has not been demonstrated in patient studies and more data is needed to determine if theophylline and beta agonists have clinically important additive effect *in vivo*.

Apparently, no development of tolerance occurs with chronic use of theophylline. The half-life is shortened with cigarette smoking. The half-life is prolonged in alcoholism, reduced hepatic or renal function, congestive heart failure, and in patients receiving antibiotics such as TAO (troleandomycin), erythromycin and clindamycin. High fever for prolonged periods may decrease theophylline elimination.

THEOPHYLLINE ELIMINATION CHARACTERISTICS

	Theophylline Clearance Rates (mean \pm S.D.)	Half-life Average (mean \pm S.D.)
Children (over 6 months of age):	1.45 \pm .58 ml/kg/min	3.7 \pm 1.1 hours
Adult nonsmokers with uncomplicated asthma	.65 \pm .19 ml/kg/min	8.7 \pm 2.2 hours

Newborn infants have extremely slow clearances and half-lives exceeding 24 hours which approach those seen for older children after about 3-6 months.

Older adults with chronic obstructive pulmonary disease, any patients with cor pulmonale or other causes of heart failure, and patients with liver pathology may have much lower clearances with half-lives that may exceed 24 hours.

The half-life of theophylline in smokers (1 to 2 packs/day) averaged 4-5 hours among various studies, much shorter than the half-life in non-smokers who averaged about 7-9 hours. The increase in theophylline clearance caused by smoking is probably the result of induction of drug-metabolizing enzymes that do not readily normalize after cessation of smoking. It appears that between 3 months and 2 years may be necessary for normalization of the effect of smoking on theophylline pharmacokinetics.

INDICATIONS: For relief and/or prevention of symptoms from asthma and reversible bronchospasm associated with chronic bronchitis and emphysema.

CONTRAINDICATIONS: In individuals who have shown hypersensitivity to any of its components.

WARNINGS: Status asthmaticus is a medical emergency. Optimal therapy frequently requires additional medication including corticosteroids when the patient is not rapidly responsive to bronchodilators.

Excessive theophylline doses may be associated with toxicity, and serum theophylline levels are recommended to assure maximal benefit without excessive risk. Incidence of toxicity increases at levels greater than 20 mcg/ml. Morphine, curare, and stilbamidine should be used with caution in patients with airflow obstruction since they stimulate histamine release and can induce asthmatic attacks. They may also suppress respiration leading to respiratory failure. Alternative drugs should be chosen whenever possible.

There is an excellent correlation between high blood levels of theophylline resulting from conventional doses and associated clinical manifestations of toxicity in (1) patients with lowered body plasma clearances (due to transient cardiac decompensation), (2) patients with liver dysfunction or chronic obstructive lung disease, (3) patients who are older than 55 years of age, particularly males.

There are often no early signs of less serious theophylline toxicity such as nausea and restlessness, which may appear in up to 50 percent of patients prior to onset of convulsions. Ventricular arrhythmias or seizures may be the first signs of toxicity.

Many patients who have higher theophylline serum levels exhibit a tachycardia. Theophylline products may worsen pre-existing arrhythmias.

USAGE IN PREGNANCY: Safe use in pregnancy has not been established relative to possible adverse effects on fetal development, but neither have adverse effects on fetal development been established. This is, unfortunately, true for most antiasthmatic medications. Therefore, use of theophylline in pregnant women should be balanced against the risk of uncontrolled asthma.

PRECAUTIONS: Mean half-life is shorter in smokers than in non-smokers, therefore, smokers may require larger doses of theophylline. Theophylline should not be administered concurrently with other xanthine medications. Use with caution in patients with severe cardiac disease, severe hypoxemia, hypertension, hyperthyroidism, acute myocardial injury, cor pulmonale, congestive heart failure, liver disease, and in the elderly (especially males), and in neonates. Great caution should especially be used in giving theophylline to patients in congestive heart failure. Such pa-

tients have shown markedly prolonged theophylline blood level curves with theophylline persisting in serum for long periods following discontinuation of the drug.

Use theophylline cautiously in patients with history of peptic ulcer. Theophylline may occasionally act as a local irritant to G.I. tract although gastrointestinal symptoms are more commonly central and associated with serum concentrations over 20 mcg/ml.

ADVERSE REACTIONS: The most consistent adverse reactions are usually due to overdose and are:

1. Gastrointestinal—nausea, vomiting, epigastric pain, hematemesis, diarrhea.
2. Central nervous system—headaches, irritability, restlessness, insomnia, reflex hyperexcitability, muscle twitching, clonic and tonic generalized convulsions.
3. Cardiovascular—palpitation, tachycardia, extrasystoles, flushing, hypotension, circulatory failure, life threatening ventricular arrhythmias.
4. Respiratory—tachypnea.
5. Renal—albuminuria, increased excretion of renal tubular cells and red blood cells, potentiation of diuresis.
6. Others—hyperglycemia and inappropriate ADH syndrome.

DRUG INTERACTIONS: Toxic synergism with ephedrine has been documented and may occur with some sympathomimetic bronchodilators.

Drug	Effect
Aminophylline with Lithium Carbonate	Increased excretion of Lithium Carbonate
Aminophylline with Propranolol	Antagonism of Propranolol effect
Theophylline with Furosemide	Increased Diuresis of Furosemide
Theophylline with Hexamethonium	Decreased Hexamethonium-induced chronotropic effect
Theophylline with Reserpine	Reserpine-induced Tachycardia
Theophylline with Chlordiazepoxide	Chlordiazepoxide-induced fatty acid mobilization
Theophylline with Cyclamycin, TAO (troleandomycin), Erythromycin, Lincomycin	Increased Theophylline plasma levels

OVERDOSAGE: Management:

- A. If potential oral overdose is established and seizure has not occurred:
 - 1) Induce vomiting.
 - 2) Administer a cathartic (this is particularly important if sustained release preparations have been taken).
 - 3) Administer activated charcoal.
- B. If patient is having a seizure:
 - 1) Establish an airway.
 - 2) Administer O_2 .
 - 3) Treat the seizure with intravenous diazepam, 0.1 to 0.3 mg/kg up to 10 mg.
 - 4) Monitor vital signs, maintain blood pressure and provide adequate hydration.
- C. Post-Seizure Coma:
 - 1) Maintain airway and oxygenation.
 - 2) If a result of oral medication, follow above recommendations to prevent absorption of drug, but intubation and lavage will have to be performed instead of inducing emesis, and the cathartic and charcoal will need to be introduced via a large bore gastric lavage tube.
 - 3) Continue to provide full supportive care and adequate hydration while waiting for drug to be metabolized. In general, the drug is metabolized sufficiently rapidly so as to not warrant consideration of dialysis.
- D. Animal studies suggest that phenobarbital may decrease theophylline toxicity. There is as yet, however, insufficient data to recommend pre-treatment of an overdose with phenobarbital.

DOSE AND ADMINISTRATION: Therapeutic serum levels associated with optimal likelihood for benefit and minimal risk of toxicity are considered to be between 10 mcg/ml and 20 mcg/ml. Levels above 20 mcg/ml may produce toxic effects. There is great variation from patient to patient in dosage needed in order to achieve a therapeutic blood level because of variable rates of elimination. Because of this wide variation from patient to patient, and the relatively narrow therapeutic blood level range, dosage must be individualized and monitoring of theophylline serum levels is highly recommended.

Dosage should be calculated on the basis of lean (ideal) body weight where mg/kg doses are stated. Theophylline does not distribute into fatty tissue.

Giving theophylline with food may prevent the rare case of stomach irritation; and though absorption may be slower, it is still complete.

Usual Initial Dose: The average initial children's (under 9 years of age) dose is one SUSTAIRE (theophylline, anhydrous) 100 mg tablet q12h.

The average initial children's (ages 9-12) dose is one-half (150 mg) of a SUSTAIRE 300 mg tablet q12h.

The average initial adolescent (ages 12-16) dose is two SUSTAIRE 100 mg tablets q12h.

The average initial adult dose is one SUSTAIRE 300 mg tablet q12h.

If the desired response is not achieved with the above AVERAGE INITIAL DOSAGE recommendation, and there are no adverse reactions, the dose may be safely increased by 2-3 mg per kg body weight per day at 3 day intervals until the following dose schedule or a maximum of 900 mg in any 24 hour period is attained (whichever is less). (See table below.)

MAXIMUM DOSE WITHOUT MEASUREMENT OF SERUM CONCENTRATION

	mg per kg body weight*	dose per interval
Children (under 9)	24 mg per day	12 mg q12h**
Children (9-12)	20 mg per day	10 mg q12h
Adolescents (12-16)	18 mg per day	9 mg q12h
Adults	13 mg per day	6.5 mg q12h

*Use ideal body weight for obese patients

**Some children under 9 may require 8 mg q8h

If higher doses than those contained in the above dose schedule are necessary, it is recommended that serum theophylline levels be monitored as a clinical guide.

Measurement of serum theophylline concentration during chronic therapy: If the above maximum doses are to be maintained or exceeded, serum theophylline measurement is recommended. This should be obtained at the approximate time of peak absorption during chronic therapy with SUSTAIRE. SUSTAIRE produces relatively flat serum theophylline level curves and serum theophylline levels may be measured at any time during the dosing cycle. However, peak levels usually occur between 4 and 8 hours after dosing. It is important that the patient will have missed no doses during the previous 48 hours and that dosing intervals will have been reasonably typical with no added doses during that period of time.

HOW SUPPLIED: SUSTAIRE 100 mg and 300 mg Sustained Release scored tablets are available in bottles of 100.

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VARIATIONS IN DOSE AND TIME OF COLLAGENASE DIGESTION FOR MAXIMAL ISLET CELL SEPARATION FOR TRANSPLANTATION

Luis H. Toledo Pereyra, MD, PhD

Summary: This work attempts to define the ideal amount and time of collagenase digestion required for islet cell separation for portal vein transplantation in the rat. Collagenase used in doses of 40-80 mg for 5 to 10 minutes of digestion at 37° C appeared at least to be as good as the initial amount of collagenase utilized (8 mg for 20 minutes at 37° C) for islet cell separation.

Resumen: Este trabajo estudia la cantidad ideal de colagenasa que debe utilizarse para la separación de islotes antes del transplante en la vena porta de la rata. Nuestro estudio parece indicar que 40 a 80 mg de colagenasa por 5 a 10 minutos a 37° C es posiblemente tan buena como la separación obtenida con 8 mg de colagenasa por 20 minutos a 37° C, que es la cantidad que rutinariamente se ha utilizado para los trasplantes de islotes en la rata.

Early work in islet cell transplantation showed that 50-60 mg of collagenase were necessary to obtain good separation of functional islet cells in the rat (1). These initial doses of collagenase were modified in order to improve the islet cell yield and the glycemic response post-transplantation (2, 3). Recent lots of collagenase have not been tested in terms of the ideal concentration and considerable variation as to the optimal dose for islet cell separation has been reported (1-3). Our work attempts to define the ideal amount and time of collagenase digestion required for islet cell separation.

Material and Methods

Pancreases obtained from adult male Lewis rats were minced into 1-2 mm pieces, the pancreatic tissue was digested at 37° C for variable periods of time (5, 10, 15, and 20 minutes) with 8, 40, or 80 mg of collagenase per pancreas (Worthington Type IV, lot No. 48K186, 190 U/mg). Tissue insulin and amylase released in the supernants were determined prior to and after collagenase digestion. After digestion, the tissue was dissociated by the Ficoll gradient separation technique (4). Separated islets were counted under the microscope and injected into the portal vein of recipient animals which underwent streptozotocin (65 mg/K) (Upjohn Company) induced diabetes. Immediately after transplantation, the ani-

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TABLE I
General Characteristics of all groups treated with various amounts of collagenase
for different periods of digestion

GROUPS *		Amylase released ** (U/ml/pancreas) ($M \pm SD$) ¹	Insulin released ** (μ U/ml/pancreas) ($M \pm SD$)	Normoglycemia (< 120 mg/dl) obtained with islets recovered from ≤ 6 donors
8 mg collagenase minutes of digestion				
I.	5	19,578 ± 3,969	1,534 ± 749	--
II.		32,652 ± 5,182	2,872 ± 1,036	--
III.	15	28,548 ± 5,873	2,504 ± 978	+
IV.	20	24,275 ± 6,175	2,435 ± 883	+
40 mg collagenase minutes of digestion				
V.	5	24,641 ± 5,275	9,863 ± 2,064	--
VI.	10	30,287 ± 4,872	8,275 ± 1,272	∇
VII.	15	21,833 ± 5,194	10,384 ± 1,878	--
VIII.	20	24,576 ± 4,249	12,863 ± 2,329	--
80 mg collagenase minutes of digestion				
IX.	5	32,368 ± 5,645	11,536 ± 2,633	^o
X.	10	27,676 ± 4,234	14,462 ± 3,071	^o
XI.	15	24,538 ± 5,349	12,547 ± 4,264	--
XII.	20	26,487 ± 5,491	15,681 ± 3,647	--

* - six recipient animals were included per each group. Islets obtained from six donors pancreases were transplanted into each recipient, unless otherwise indicated.

** - amylase or insulin released in the supernatant after collagenase digestion.

∇ - normoglycemia obtained with islets recovered from 5 donors.

^o - normoglycemia obtained with islets recovered from 4 donors.

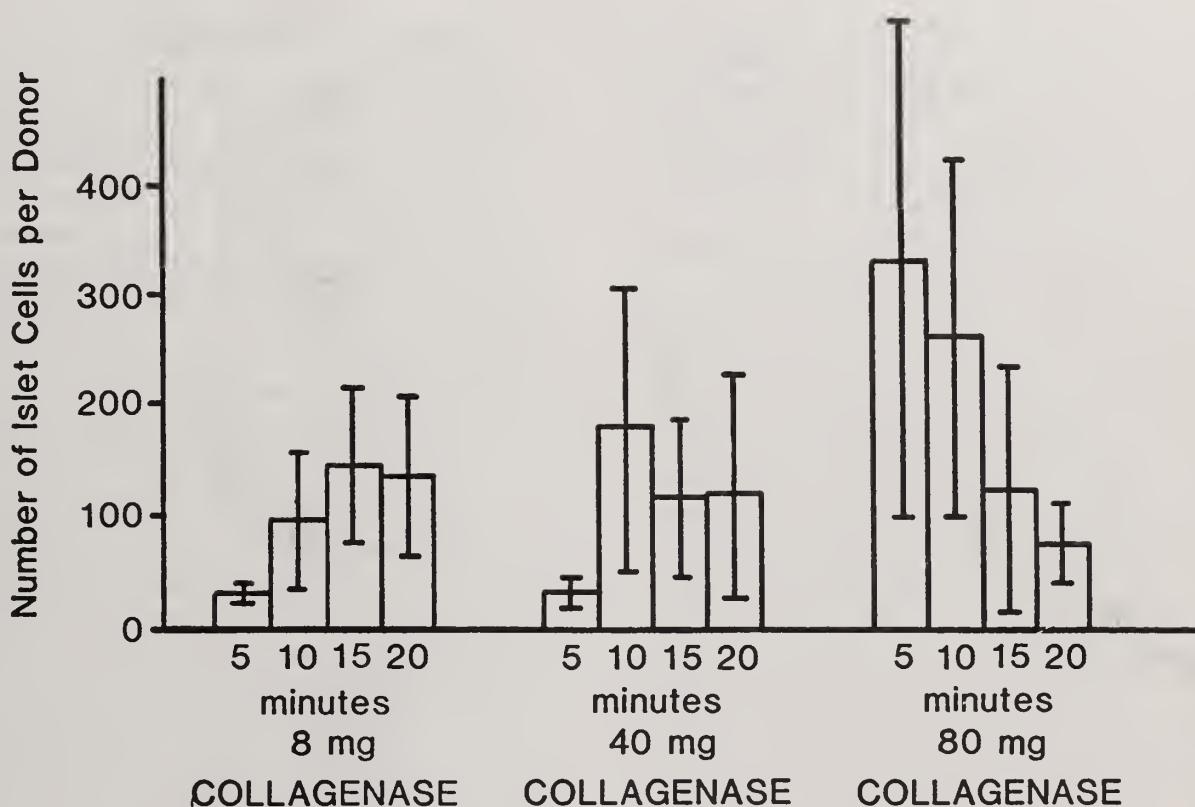


Figure 1: Amount of islet cells isolated in the various groups of collagenase treated pancreases. Each time variation in each one of the collagenase treated groups represents the mean \pm SD of the number of islet cells obtained from twenty-four to thirty-six donor pancreases. Low doses of collagenase required higher times of digestion, whereas the high dose groups required shorter times of digestion.

mals were followed for a period of three months. Table I indicates the various groups studied. Six recipient animals were included per each group. Six donors per recipient were utilized, unless otherwise specified. The statistical analysis with Student's t-test and analysis of variance method was carried out for all variables.

Results

Figure 1 shows the number of islets isolated per donor in the various collagenase

groups. Although the best time of collagenase digestion for the 8 mg dose was 15 minutes, this time of digestion was only statistically ($p > 0.05$) different to the 5 minutes digestion time. It was interesting to see that once the dose of collagenase was increased, the ideal time of collagenase digestion was proportionately decreased. For instance, in the 40 mg of collagenase group, ten minutes digestion time was the optimal time; whereas, 15 and 20 minutes digestion decreased considerably the number of islets. The 80 mg of collagenase

group showed the same phenomena seen in the 40 mg group. Five minutes of collagenase digestion with 80 mg was better for islet cell isolation than longer periods of time at lower doses. These values, however, were not statistically ($p < 0.08$) different.

Table I shows the general characteristics of all groups of collagenase treated islets. The amount of amylase released into the supernatant was a reflection of the amount of exocrine tissue destroyed during the process of collagenase treatment. Increased release of amylase in the supernatant was proportional to purified islet cell tissue. The amount of insulin released into the supernatant was most likely a reflection of the amount of islet cells destroyed during collagenase treatment or also might simply represent degranulation of otherwise viable islets. Nevertheless, the insulin level in the supernatant was inversely proportional to the potential insulin left in the tissue after collagenase treatment. Although the changes observed among the different groups appear to be real, there were no statistical ($p > 0.08-0.5$) differences.

Normoglycemia after transplantation of islets recovered from six donors was seen only in the groups treated with 8 mg of collagenase for 15 to 20 minutes, 40 mg of collagenase for 10 minutes and 80 mg of collagenase for 5 or 10 minutes. In fact, the best group was the one treated with 80 mg of collagenase and five minutes of digestion which required islets obtained from four donors to produce normoglycemia (Table I).

Comments

Our study appears to indicate that 8 mg of collagenase after 15 to 20 minutes of digestion is not the only satisfactory way to separate islet cells. It also appears that higher

concentrations of collagenase with less time of digestion would offer an increased number of islet cells, as well as an increased purified islet cell mass. It has been indicated on empirical basis that 8-15 mg of collagenase for 20 minutes digestion is the optimal concentration and time for islet cell separation for transplantation. Workers in the field of islet cell transplantation have soon realized that the amount of collagenase utilized mainly depended on the activity and lot of collagenase used for islet cell separation. This study indicates that 8 mg of collagenase for 20 minutes is not the only and best treatment for maximal islet cell separation. Recently, Kretschmer and his associates (3) demonstrated that 600 U of collagenase/ml of tissue was the ideal amount for 20 minutes digestion of canine islet cells not subjected to the Ficoll gradient separation technique. Utilizing equivalent amounts of collagenase obtained from a different lot, we did not obtain the same results in the rat.

Our studies appear to indicate that there is an inverse relationship between amount of collagenase and time of digestion. Low doses of collagenase required more digestion, whereas, high doses of collagenase needed minimal digestion time. It appears, therefore, that 40-80 mg of collagenase used for tissue digestion for 5-10 minutes was probably as good as the 8 mg of collagenase for 20 minutes of digestion. A precise correlation of these figures would allow for a better utilization of collagenase digestion prior to separation or islet cell transplantation.

Acknowledgments

The laboratory and editorial help from P. Cromwell and S. E. Malcolm in the development of this work is appreciated.

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Smith GR et al: *Psychosomatics* 15 138, 3rd quarter, 1974

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Tobin JM et al: *Geriatrics* 25(6):122, 1970

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Bernstein JG: *Clinical Psychopharmacology*
Littleton, MA, PSG Publishing Company, 1978, p 123

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Bernstein JG: *Management of Side Effects Related to Antipsychotic Drug Therapy* An Interview, 1978, p 12

*Although some instances of drowsiness have been reported, marked sedation is rare.

**Transient hypotension occurs rarely; severe orthostatic hypotension has not been reported.

Note: Extrapyramidal symptoms, when they occur, are readily controllable with antiparkinson drugs or dosage adjustment.

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Summary of Prescribing Information

Contraindications: Severe depression, coma, CNS depression due to centrally-acting depressants, Parkinson's disease, hypersensitivity to the drug

Warnings: Usage in Pregnancy: Safe use in pregnancy or in women likely to become pregnant has not been established; use only if benefit clearly justifies potential hazards. Infants should not be nursed during drug treatment.

Usage in Children: Safety and effectiveness not established, not recommended in pediatric age group.

Combined Use With Lithium: Patients receiving lithium plus haloperidol should be monitored closely for early evidence of neurological toxicity.

General: Bronchopneumonia, sometimes fatal, has followed use of major tranquilizers, including haloperidol. Prompt remedial therapy should be instituted if dehydration, hemoconcentration or reduced pulmonary ventilation occurs, especially in the elderly. Decreased serum cholesterol and/or cutaneous and ocular changes have been reported with chemically-related drugs, although not with haloperidol. Mental and/or physical abilities required for hazardous tasks or driving may be impaired. Alcohol should be avoided due to possible additive effects and hypotension.

Precautions: Administer cautiously to patients: (1) with severe cardiovascular disorders, due to the possibility of transient hypotension and/or precipitation of anginal pain (if a vasopressor is required, epinephrine should not be used since HALDOL haloperidol may block its vasopressor activity and paradoxical further lowering of blood pressure may occur); (2) receiving anticonvulsant medication since HALDOL haloperidol may lower the convulsive threshold; (3) with known allergies or a history of allergic reactions to drugs; (4) receiving anticoagulants. Concomitant antiparkinson medication, if required, may have to be continued after HALDOL haloperidol is discontinued because of different excretion rates; if both are discontinued simultaneously, extrapyramidal symptoms may occur. Intraocular pressure may increase when anticholinergic drugs, including antiparkinson drugs, are administered concomitantly with HALDOL haloperidol. When HALDOL haloperidol is used for mania in cyclic disorders, there may be a rapid mood swing to depression. Severe neurotoxicity may occur in patients with thyrotoxicosis receiving antipsychotic medication, including HALDOL haloperidol.

Adverse Reactions: CNS Effects: Extrapyramidal Reactions: Neuromuscular (extrapyramidal) reactions have been reported frequently, often during the first few days of treatment. Generally they involved Parkinson-like symptoms which were usually mild to moderately severe and usually reversible. Other types of neuromuscular reactions (motor restlessness, dystonia, akathisia, hyperreflexia, opisthotonos, oculogyric crises) have been reported far less frequently, but were often more severe. Severe extrapyramidal reactions have been reported at relatively low doses. Generally, extrapyramidal symptoms are dose-related since they occur at relatively high doses and disappear or become less severe when the dose is reduced. Antiparkinson drugs may be

required. Persistent extrapyramidal reactions have been reported and the drug may have to be discontinued in such cases.

Withdrawal Emergent Neurological Signs: Abrupt discontinuation of short-term antipsychotic therapy is generally uneventful. However, some patients on maintenance treatment experience transient dyskinetic signs after abrupt withdrawal. In certain cases these are indistinguishable from "Persistent Tardive Dyskinesia" except for duration. It is unknown whether gradual withdrawal will reduce the occurrence of these signs, but until further evidence is available haloperidol should be gradually withdrawn.

Persistent Tardive Dyskinesia: Although rarely reported with HALDOL haloperidol, tardive dyskinesia may appear during or after long-term therapy. The risk appears to be greater in elderly patients on high-dose therapy, especially females. Symptoms are persistent and sometimes appear irreversible, there is no known effective treatment and all antipsychotic agents should be discontinued. The syndrome may be masked by reinstitution of drug, increasing dosage, or switching to a different antipsychotic agent.

Other CNS Effects: Insomnia, restlessness, anxiety, euphoria, agitation, drowsiness, depression, lethargy, headache, confusion, vertigo, grand mal seizures, and exacerbation of psychotic symptoms.

Cardiovascular Effects: Tachycardia and hypotension. **Hematologic Effects:** Reports of mild, usually transient leukopenia and leukocytosis, minimal decreases in red blood cell counts, anemia, or a tendency toward lymphomonocytosis; agranulocytosis rarely reported and only in association with other medication.

Liver Effects: Impaired liver function and/or jaundice reported. **Dermatologic Reactions:** Maculopapular and acneiform reactions, isolated cases of photosensitivity, loss of hair.

Endocrine Disorders: Lactation, breast engorgement, mastalgia, menstrual irregularities, gynecomastia, impotence, increased libido, hyperglycemia and hypoglycemia.

Gastrointestinal Effects: Anorexia, constipation, diarrhea, hypersalivation, dyspepsia, nausea and vomiting. **Autonomic Reactions:** Dry mouth, blurred vision, urinary retention and diaphoresis. **Respiratory Effects:** Laryngospasm, bronchospasm and increased depth of respiration.

The injectable form is intended only for acutely agitated psychotic patients with moderately severe to very severe symptoms.

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Answers:

1. Answer is C. Levels of lactic acid greater than 35 mg/dl in the CSF are consistently associated with bacterial or tuberculous meningitis, whereas levels less than 35 mg/dl are consistently associated with non-bacterial infections (presumably viral) or the absence of infection.

Reference: *Journal of Infectious Diseases* 137: 384, 1978.

2. Answer is D. Patients with sickle cell disease, asplenia, and multiple myeloma are prone to pneumococcal sepsis. Patients with the rare condition of chronic granulomatous disease of childhood are able to phagocytize and kill *only* those organisms which do *not* produce catalase, e. g. members of the streptococcus family (including pneumococcus).

Reference: *NEJM* 298: 721, 1978.

3. Answer is C. Retinochoroiditis is seen most often as a late sequel to *congenital* toxoplasmosis. As manifestation of *acquired* disease, this condition is so rare that it is reportable.

Reference: *American Journal of Medicine* 64: 396, 1978.

4. Answer is A. Protozoa infections (unicellular parasites) do not cause eosinophilia, whereas infections due to helminths, nematodes, and trematodes may cause marked eosinophilic responses.

Reference: Plorde JJ: *Amebiasis*, *Harrison's Principles of Internal Medicine*, 8th ed, Thorn et al, eds, McGraw-Hill, 1977.

5. Answer is E. A number of infectious and non-infectious diseases can cause suppression of cell-mediated immunity.

Reference: *NEJM* 298: 21, 1978.

6. Answer is C. A trial of daily low-dose doxycycline in Peace Corps workers significantly diminished the incidence of travelers' diarrhea.

Reference: *NEJM* 298: 758, 1978.

7. Answer is B. Staphylococci are by far the most common organisms causing endocarditis in intravenous drug users. Any initial antibiotic regimen must contain a penicillinase-resistant penicillin (or its equivalent in the penicillin-allergic patient).

Reference: *Southern Medical Journal* 71: 638, 1978.

8. Answer is D. There is an extremely high association of *S. bovis* septicemia and cancers of the gastrointestinal tract. *S. bovis* frequently causes endocarditis and is exquisitely sensitive to penicillin, so that the addition of an aminoglycoside is unnecessary.

Reference: *Ann In Med* 91: 560, 1979.

9. Answer is E. As many as 90 to 95 per cent of cases of post-transfusion hepatitis may be due to non-A, non-B hepatitis agent. Screening has greatly reduced the prevalence of hepatitis B, which formerly was the most common offender.

Reference: *Gastroenterology* 75: 736, 1978.

10. Answer is B. There is good evidence that prompt, adequate (10 days) therapy with penicillin markedly reduces the incidence of post-streptococcal acute rheumatic fever. There is no such data for post-streptococcal glomerulonephritis. The ASO titer is most often elevated after streptococcal pharyngitis, while the titer of anti-DNAase B is high after impetigo. There are no group A strains of streptococcus resistant to penicillin.

Reference: *NEJM* 297: 311; 365, 1977.

11. Answer is B. Pneumocystis occurs almost exclusively in severely immunocompromised hosts receiving steroids or chemotherapy. The disease is almost uniformly fatal if untreated. Recent experience with prophylactic trimethoprim-sulfamethoxazole in children undergoing chemotherapy for leukemia indicates a marked reduction in the incidence of *Pneumocystis carinii* pneumonia. The only effective way to make the diagnosis is by lung biopsy.

Reference: *NEJM* 297: 1381, 1977.

12. Answer is A. The child most likely has Reye's syndrome, a complex of hepatic failure and cerebral edema occurring after minor systemic infections, such as influenza or varicella. Hypoglycemia has also been reported with Reye's syndrome, particularly in the later stages. Therefore, tests for serum glucose, SGOT, bilirubin, and prothrombin time should be ordered immediately, along with measures to reduce cerebral edema. Papilledema and the absence of nuchal rigidity also suggest increased intracranial

pressure rather than meningitis. In any case, lumbar puncture is contraindicated in the presence of papilledema, because of the danger of herniation through the foramen magnum. Barium swallow is contraindicated in view of the vomiting and obtunded state.

Reference: *American Journal of Diseases of Children* 128: 36, 1974.

13. Answer is C. Recent experiments have shown that *Clostridium difficile* is the causative agent in laboratory animals, and some human studies have shown similar results. Vancomycin has been effective in treating the majority of patients. The diagnosis is made by observing the typical pseudomembrane on the colonic mucosa by sigmoidoscopy. However, many antibiotics—not just clindamycin—have been implicated as causes of the syndrome, including ampicillin, tetracycline, and cephalothin.

Reference: *NEJM* 298: 531, 1978.

14. Answer is E. There are many manifestations of Mycoplasma infections which are not due to the pneumonia per se. Only a few are listed here.

Reference: *Medical Clinics of North America* 62: 961, 1978.

15. Answer is A. All of the organisms except pneumococcus have been shown to produce a penicillinase compound. There have been some recent reports from overseas of pneumococcal resistance to penicillin, but the beta-lactamase enzyme was *not* found to be the mechanism in

these cases. It is theorized that such resistance is gained ready-made via chromosomal "resistance transfer factors" (R plasmins) obtained during conjugation

with penicilin-resistant organisms.

Reference: *Infectious Diseases*, 2nd edition, p. 175.
Kucers A and Bennett N: *The Uses of Antibiotics*, Lippincott, 1979, p. 4.

SEXUALLY TRANSMITTED DISEASES

PART I

GONOCOCCAL INFECTIONS

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Introduction

During the month of January 1980, a new center for the diagnosis and treatment of sexually transmitted diseases (STD) was inaugurated in the Puerto Rico Medical Center. We felt it was necessary to review the most frequent STD. STD are not class conscious and are seen frequently (1).

The five classic sexually transmitted diseases are gonorrhea, syphilis, chancroid, lymphogranuloma venereum and granuloma inguinale (2-5, 5A, 5B). The latter three diseases have become uncommon at the present time. In contrast, other sexually transmitted agents have begun to appear. Tables I and II, respectively, list the sexually transmitted diseases seen in persons attending STD clinics in some areas of the United States as contrasted with those causes for admission to STD clinic in Scandinavia (6, 6A).

Numerically, gonorrhea and non-specific urethritis constitute the major problems in these clinics. Other significant problems include syphilis, genital herpes, pediculosis,

scabies, trichomiasis, candidiasis, non-specific vaginitis, molluscum contagiosum and condyloma acuminata. The listings do not tabulate such pathogens as cytomegalovirus which are known, in part, to be sexually transmitted (7-9). The tables do not include some of the problems encountered by the homosexual population (3). In gay men, for example, hepatitis B virus is a major pathogen with an attack rate that may average 5 percent per year (10, 11). Other pathogens affecting the gay male population include enteric microorganisms such as amebiasis, giardiasis, salmonellosis (3). A broader concept of sexually transmitted diseases is beginning to emerge. We will discuss the most frequent ones and refer you to broader reviews for the minor ones. We will not attempt to discuss the social aspects of STD or the reasons for their epidemic proportions (12, 13).

Neisseria Gonorrhoeae

The organisms and clinical correlations

Neisseria Gonorrhoeae, the gonococcus, is a pathogen known to mankind since the beginning of recorded history. The microorganism has a particular capacity to affect columnar epithelial tissue (14, 15). In uncomplicated gonorrhea in the male, the gonococcus must ascend the urethra against the normal clearing mechanisms of the downward flow

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of mucous and urine. The initial stage in the disease process involves attachment of the microorganism to the microvilli of the columnar epithelial cells followed by penetration into the cell, multiplication and finally entrance into the subepithelial tissue. In its attachment and passage through the columnar epithelium, the gonococcus incites an inflammatory response in which polymorphonuclear leucocytes predominate. The clinical and pathological picture of gonorrhea results from the combination of these processes culminating in an inflamed, denuded urethral epithelium along with the presence of many leucocytes (16, 17). The gonococcus in the male generally causes anterior urethritis but it can cause posterior urethritis with prostatitis and epididymitis (16). In untreated gonorrhea, there is a tendency for scar formation with urethral stricture formation as a long-known complication of the disease. In uncomplicated gonorrhea in the female, the gonococcus invades both the urethra and the endocervix (16). In 10-15 percent of gonococcal infections in the female, the microorganism finally invades the fallopian tubes destroying columnar ciliated epithelium as it passes through the opening of the tube into the area surrounding the ovary. Pelvic inflammatory disease (PID) results, sometimes followed by scar formation and infertility (22). In its disseminated form, the microorganism can cause perihepatitis (the Fitz-Hugh, Curtis syndrome) (23), the dermatitis-arthritis syndrome (disseminated gonococcal infection, DGI) and in rare instances may evenuate in meningitis and endocarditis (24). In the neonate, gonococcal ophthalmia results but the most common form of infection in this period is orogastric colonization (26). Neonatal sepsis can follow and occasionally a clinical presentation resembling the dermatitis-arthritis syndrome may result.

Pathogenetic mechanism

Recent studies have made significant advances in understanding the pathogenetic mechanisms wherein the gonococcus causes disease. It has been determined that in urethral pus, the gonococcus possesses a capsule composed most probably of polysaccharide and functioning in an antiphagocytic capacity (27, 28). In virulent gonococcal colony types (T₁, T₂, but not T₃, T₄, and T₅) for man, pili have been found extending from the surface of the bacterial cell. Their length approximates two microns; their composition is protein with a subunit molecular weight of 19,000±2,500, varying slightly for different strains (32). Gonococci can be serotyped by antigenic analysis of the pilus protein. According to one typing scheme, there are six types of gonococcal pili. Other schemes accentuate the antigenic variable determinants on pili; it has also been determined that common antigens may be found on all gonococcal pili. These structures serve as the initial site of attachment of the gonococcus to the microvilli of the columnar epithelial cell. It has been found that up to 10⁴ receptor sites for pili are present on each cervical-vaginal cell. The exact cell receptors which enable attachment of pili are not known but the structure may partially be composed of carbohydrate. Attachment of pili is enhanced at pH 4.5 and by the presence of the ferric ion at pH 7.4. Since non-piliated organisms also can be shown to attach to cells, although with less avidity, other attachment sites on the gonococcus must also exist (31). It has been suggested that the sugar moieties on gonococcal lipopolysaccharide (LPS, endotoxin) may be able to attach to the epithelial cell directly (34). Gonococcal LPS was incorporated into the membrane of artificially constructed lipo-

TABLE I
Sexually Transmissible Diseases (STD) in Men, STD Clinic
October 1, 1976- June 30, 1977

	Cases per 100 Visits by Men					
	New Haven	Detroit	Minneapolis	Denver	Dekalb	Lexington
Gonorrhea	22.3	44.4	20.9	20.1	22.4	36.7
Nongonococcal Urethritis	29.5	25.1	24.6	27.6	24.4	4.2
Genital herpes	2.7	0.1	4.3	3.0	7.3	1.7
Venereal warts						
Venereal warts	1.0	0.1	4.6	5.5	6.5	2.2
Syphilis	2.5	2.2	1.8	1.2	1.3	3.3
Scabies	2.2	0.0	1.8	1.0	2.4	0.6
Pediculosis Public	4.5	0.4	2.1	4.3	1.8	2.5
All Other *	0.8	0.3	0.3	2.1	2.2	0.1
Total	65.5	72.6	60.4	64.8	68.3	51.3
Total visits	1,900	2,178	6,811	8,919	2,455	1,535

* Includes (cases per 100 visits): molluscum contagiosum (1.0), chancroid (0.1), lymphogranuloma venereum (< 0.1), and granuloma inguinale (0.0)

somes with the immunodeterminants expressed at the liposomal surface. Liposomes containing gonococcal LPS were able to attach more readily to epithelial cells than control liposomes.

After attachment has been accomplished, the gonococcus is endocytosed by the epithelial cell. Multiplication of the micro-organism takes place within the lumen, on

the surface of the epithelial cell and within the interior of the cell. Finally, the micro-organism penetrates into subepithelial tissue, initiating inflammatory changes and destroying the epithelial cells. The mechanisms wherein the cells are destroyed probably mostly involve gonococcal LPS and other toxins, incompletely characterized at present (34). In addition to carrying LPS, the outer cell mem-

TABLE II

Diagnoses Recorded in Per Cent at the VD Clinic, 1972

	Men (n=2,090)	Women (n=1,489)
<i>Gonorrhoeae</i>	23.0	33.0
<i>Syphilis</i>	0.5	0.3
<i>T. vaginalis</i>	1.0	10.0
<i>C. albicans</i>	4.0	20.0
<i>Condyloma ac.</i>	8.0	5.0
<i>Herpes sx. gen.</i>	2.6	1.8
<i>Pedicnlosis</i>	2.0	2.1
<i>Scabies</i>	0.9	0.3
<i>Non-gon. urethritis</i>	33.0	4.0
<i>Non-gon. vaginitis</i>	----	10.0
<i>Various</i>	6.0	3.0
<i>Observation</i>	26.0	23.0
<i>Total percentages</i>	107.0	112.5

brane contains a mixture of proteins (1a, 2 and 3). Protein 1, the principal outer membrane protein (POMP), exists in two principal forms, 1a and 1b, but both forms are antigenically alike. Protein 2 is also expressed on the cell surface (29). The original gonococcal typing scheme of Johnston and Gottschlich used an outer membrane protein complex, consisting of LPS, protein 1 and 2, and determined there were 16 serotypes of *Neisseria gonorrhoeae* (33).

Gonococcal resistance to antibiotics.

Underneath the outer cell membrane is the peptidoglycan cell wall. Changes in cell wall linking resulting in permeability differences occur on a genetic basis and account for low level resistance to multiple antibiotics. The inner cell membrane encloses ribosomal elements, mitochondria and genetic information. The genetic information is in the form of chromosomal and plasmid DNA (35,35A). It has been determined that there may be as many as three plasmids in the gonococcus (36). the intermediate sized plasmid has been determined to be that portion of

DNA which codes for the production of penicillinase. It has been ascertained by DNA homology studies that the intermediate sized plasmid most probably was inserted into the gonococcus by conjugation with *Hemophilus parainfluenzae* under intense antibiotic pressure in several different parts of the world (Far East, West Africa). This plasmid is present only in penicillinase producing gonococci (32). The function of the smallest plasmid is not known and for that reason it has been termed the "cryptic" plasmid. The largest plasmid is thought to code for structures involved in the process of conjugation. Although penicillinase production is one method of antibiotic resistance, microorganisms producing this enzyme have not spread widely in the United States. Low-level antibiotic resistance, often to multiple antibiotics including penicillin, is mediated by changes in chromosomal DNA induced by the pressure of antibiotic concentrations insufficient to kill the gonococcus. According to Sparling, in the presence of a suboptimal concentration of antibiotic, changes in chromosomal DNA occur (35). These changes result in increased cross-linking of the peptidoglycan cell wall and to alterations of the outer cell membrane proteins. As a consequence, there is decreased permeability of the outer surface of the gonococcus making it more difficult for multiple antibiotics including penicillin to cross into the interior of the cell. As a consequence of these changes, the gonococcus survives in a hostile environment. The microorganism, however, is not able to compete with antibiotic sensitive gonococci when the selective pressure of inadequate antibiotic dosage is removed. Prior to the widespread use of relatively high dose penicillin usage as recommended by the USPHS, the gonococcus was becoming increasingly resistant to multiple antibiotics. After 1972, this trend was reversed with penicillin sensitive gonococci be-

coming more prevalent (35).

Immunology of gonococcal infections.

Much also has been learned about the immunology of gonococcal infections. Polymorphonuclear leucocytes are brought to the epithelial surface by gonococcal products called chemotaxins (38). At the epithelial surface, both IgG and secretory IgA are formed in response to infection (39-42). The IgA most probably functions to coat gonococcal surface antigens thereby preventing attachment. Gonococci also produce a protease which is capable of splitting secretory IgA. Secretory IgA is produced by a system which has a limited immunological memory and disappears from washings of the epithelial cell surfaces relatively soon after infection has occurred (39). In the presence of immune IgG directed against the principal outer membrane protein and complement, direct lysis of the bacterial cell can occur. In the presence of immune IgG directed against gonococcal pili, phagocytosis is enhanced (opsonic phagocytosis). It is misleading to consider that all gonococci that are encountered in urethral pus are intracellular. In phase microscopy studies, it can be seen that some of these gonococci actually rest on the surface of the cell. Once inside the phagocyte, the gonococcus is destroyed (38). Without specific antibiotic therapy, gonococcal mucosal infections are limited in time. Recurrent mucosal infections are common and result from the antigenic diversity of the gonococcus aided by the limited memory of the surface immunoglobulin secretory system. Although recurrent mucosal infections are common, a documented second episode of disseminated gonococcal infection is distinctly uncommon and should signal the physician to investigate the patient for a disorder of one of the terminal components of complement (C6

through C8) (43).

Pelvic inflammatory disease.

The pathogenesis of pelvic inflammatory disease (PID) is being elucidated (44). It has been hypothesized that initial episodes of PID are related to infection with the gonococcus. First episodes predispose to recurrent infections by disturbing surface mucosal immunity by scar formation and disruption of the normal ciliated columnar epithelium of the endosalpinx. In cultures of women with PID taken by culdocentesis, multiple microorganisms, with and without the gonococcus can be found (45-47). Even in first episodes of PID, the gonococcus may only be found in the endocervix. It appears probably that gonococcal infection predisposes to invasion of the endosalpinx by normal genital tract commensals. Secondary or tertiary episodes of PID are more completely caused by these commensals. An alternate explanation that seems less likely is that the gonococcus may initiate all episodes of PID, with the absence of that microorganism from culdocentesis cultures being a function of the time elapsed from the beginning of the infection with commensal bacteria being inhibitory for the growth of the gonococcus. Inadequate treatment may cause a prolonged course of PID or lead to complications. In Scandinavian countries, the incidence of gonorrhea is decreasing. However, the incidence of PID is not and may even be increasing (48). The increase in PID in those countries has been closely correlated with the increase in non-specific urethritis. Women with PID had been cultured at laparoscopy and *Chlamydia trachomatis* has been found (49, 50). The contribution of *Chlamydia trachomatis* to PID in the United States is not known. Women with that microorganism exclusively in the endocervix

have been followed prospectively without specific therapy. Some of these patients have subsequently developed typical acute PID (51).

Disseminated gonococcal infection.

Gonococci producing DGI have been found to be distinctive (25). These microorganisms are exquisitely penicillin sensitive, are resistant to the normal bactericidal effect of human serum, have a distinctive auxotype (AHU⁻), that is, they require arginine, hypoxanthine and uracil for growth, and 88 percent of strains tested have an antigenically similar principal outer membrane protein. Episodes of DGI occur at or directly after the menses and it has been postulated that menstruation predisposes to gonococcal blood stream invasion. In the male, asymptomatic urethral and pharyngeal gonococcal colonization are often the sources of DGI (52-55). The presence of pharyngeal gonococcal colonization does not infer a homosexual preference since heterosexuals may have gonococci at this site also.

In an interesting approach toward explaining the incidence of DGI (1-3 percent of infected persons) and why the microorganism has such distinctive properties, investigators at the University of California at San Diego have recently determined that there is an antibody of the IgG class present in normal human serum that binds to the surface of DGI gonococcal strains and that subsequently prevent the binding of antibody to the gonococcus, binding of complement and bacterial cell lysis (43). This blocking antibody can be removed by absorption with DGI strains but not with other gonococcal isolates. The blocking antibody is considered unique because it appears to be the only known natural antibody which promotes bacteremia in hu-

mans.

Clinical implications of basic sciences of the gonococcus.

Much of the basic work done on the pathogenesis, microbiology and immunology of *Neisseria Gonorrhoeae* has direct clinical applicability. 1) No matter which antibiotic is given to the patient with gonorrhea, the dosage and duration should be sufficient to kill the microorganism. Inadequate dosages promote the low-level resistance to multiple antibiotics determined by increases in the impermeability of the cell wall. 2) Although penicillinase producing gonococci have not spread widely in the United States, the physician must be aware of their existence and a "test of cure", that is a culture of the patient after antibiotic treatment, should be performed on all patients after antibiotic treatment, should be performed on all patients with proven gonorrhea (56). 3) Patients particularly hard to treat are those with pharyngeal or anorectal gonorrhea, partly because penicillin does not may not attain adequate concentrations in oropharyngeal secretions and because of the potential presence of penicillinase producing microorganisms (Enterobacteriaceae) in the anorectal area. 4) Since microorganisms that cause disseminated gonococcal infection are exquisitely penicillin sensitive, they have usually been easy to treat with as little as three days of a high dose penicillin regimen (57). Some authorities continue to recommend an additional four days of antibiotic therapy. A high dose penicillin refers to 12 million units of penicillin per day for three days. 5) It may be possible to produce a vaccine against the gonococcus. The major reasons why such a vaccine could not be produced are the antigenic diversity of the gonococcus and the

limited memory of the secretory immune system at the epithelial surface where the gonococcus is most likely to be encountered first. However, a potential gonococcal vaccine might contain a mixture of the proteins which are found on pili, either multiple antigens or an antigenically, broadly, reactive constituent of the proteins found on pili. The vaccine might also contain representative principal outer membrane proteins so as to encompass the numerically most frequent gonococcal isolates in a given geographical area. Inclusion of multiple antigens in a vaccine preparation has a precedent in that the present pneumococcal vaccine contains fourteen different polysaccharide types. The pneumococcal vaccine also elicits some degree of surface immunity as determined by lower oropharyngeal colonization rates with the pneumococcus in persons given the vaccine. The gonococcal vaccine could be given to patients, for example, attending a clinic for sexually transmitted diseases.

Diagnosis of gonococcal infections.

The diagnosis of gonococcal infections in the male with urethritis is relatively simple and a gram stain of the secretions will reveal gram negative diplococci inside the polymorphonuclear leucocytes. If the urethral smear is negative, urethral cultures taken with a calcium alginate swab and plated on Thayer Martin medium should be performed. In the homosexual male cultures of the urethra, rectum and pharynx are indicated.

In the female the need for cultures of the endocervix, rectal canal and pharynx are a must. In disseminated gonococcal infection, besides the previously mentioned culture sites, blood cultures, and cultures and gram stains of the lesions should be performed (16).

Treatment of gonococcal infections (58, 59):

Uncomplicated Gonococcal Infections in Men and Women

Drug regimens of choice. Aqueous procaine penicillin G (APPG): 4.8 million units injected intramuscularly at 2 sites with 1.0 g of probenecid by mouth; OR

Tetracycline hydrochloride: 0.5 g by mouth 4 times a day for 5 days (total dosage 10.0 g). Other tetracyclines are not more effective than tetracycline hydrochloride. All tetracyclines are ineffective as a single-dose therapy; OR

Ampicillin or amoxicillin: Ampicillin, 3.5 g. or amoxicillin, 3.0 g, either one given with 1 g probenecid by mouth. Evidence shows that these regimens are slightly less effective than the other recommended regimens.

Patients who are allergic to the penicillins or probenecid should be treated with oral tetracycline as above. Patients who cannot tolerate tetracycline may be treated with spectinomycin hydrochloride, 2.0 g. in 1 intramuscular injection.

Special considerations. Single-dose treatment is preferred in patients who are unlikely to complete the multiple-dose tetracycline regimen. The APPG regimen is preferred in men with anorectal infection.

Pharyngeal infection is difficult to treat. High failure rates have been reported with ampicillin and spectinomycin.

Tetracycline treatment results in fewer cases of postgonococcal urethritis in men. It may eliminate coexisting chlamydial infections in men and women.

Patients with incubating syphilis (sero-negative, without clinical signs of syphilis) are likely to be cured by all the above regimens except spectinomycin. All patients should have a serologic test for syphilis at the time of diag-

nosis.

Patients with gonorrhea who also have syphilis or are established contacts of syphilis patients should be given additional treatment appropriate to the stage of syphilis.

Treatment of sexual partners. Men and women exposed to gonorrhea should be examined, cultured, and treated at once with one of the regimens above.

Follow-up. Follow-up cultures should be obtained from the infected site(s) 3-7 days after completion of treatment. Cultures should be obtained from the anal canal of all women who have been treated for gonorrhea.

Treatment failures. The patient who fails therapy with penicillin, ampicillin, amoxicillin, or tetracycline should be treated with 2.0 g of spectinomycin intramuscularly.

Most recurrent infections after treatment with the recommended schedules are due to *reinfection* and indicate a need for improved contact tracing and patient education. Since infection by penicillinase (β lactamase)-producing *Neisseria gonorrhoeae* is a cause of treatment failure, post-treatment isolates should be tested for penicillinase production.

Not recommended. Although long-acting forms of penicillin (such as benzathine penicillin G) are effective in syphilotherapy, they have NO place in the treatment of gonorrhea. Oral penicillin preparations such as penicillin V are not recommended for the treatment of gonococcal infection.

Penicillinase-Producing *Neisseria Gonorrhoeae* (PPNG)

Patients with uncomplicated PPNG infections and their sexual contacts should receive spectinomycin, 2.0 g., intramuscularly

in a single injection. Because gonococci are very rarely resistant to spectinomycin and reinfection is the most common cause of treatment failure, patients with positive cultures after spectinomycin therapy should be re-treated with the same dose.

A PPNG isolate that is resistant to spectinomycin may be treated with cefoxitin, 2.0 g, in a single intramuscular injection, with probenecid, 1.0 g, by mouth.

Treatment in Pregnancy

All pregnant women should have endocervical cultures for gonococci as an integral part of the prenatal care at the time of the first visit. A second culture late in the third trimester should be obtained from women at high risk of gonococcal infection.

Drug regimens of choice are APPG, ampicillin, or amoxicillin, each with probenecid as described above.

Women who are allergic to penicillin or probenecid should be treated with spectinomycin.

Refer to the sections on acute salpingitis and disseminated gonococcal infections for the treatment of these conditions during pregnancy. Tetracycline should not be used in pregnant women because of potential toxic effects for mother and fetus.

Acute Salpingitis (Pelvic Inflammatory Disease)

There are no reliable clinical criteria to distinguish gonococcal from nongonococcal salpingitis. Endocervical cultures for *N. gonorrhoeae* are essential. Therapy should be initiated immediately.

Hospitalization. In the following situa-

tions, hospitalization should be strongly considered: uncertain diagnosis, in which surgical emergencies such as appendicitis and ectopic pregnancy must be excluded; suspicion of pelvic abscess; severe illness; pregnancy; inability of the patient to follow or tolerate an outpatient regimen; or failure of the patient to respond to outpatient therapy.

Antimicrobial agents. Outpatients: *Tetracycline**: 0.5 g, taken orally 4 times a day for 10 days. This regimen should not be used for pregnant patients; OR

APPG: 4.8 million units intramuscularly, ampicillin, 3.5 g, or amoxicillin, 3.0 g., each with probenecid, 1.0 g. Either regimen is followed by ampicillin, 0.5 g, or amoxicillin, 0.5 g, orally 4 times a day for 10 days.

Hospitalized patients: *Aqueous crystalline penicillin G*: 20 million units given intravenously each day until improvement occurs, followed by ampicillin, 0.5 g, orally 4 times a day to complete 10 days of therapy; OR

*Tetracycline**: 0.25 g. given intravenously 4 times a day until improvement occurs, followed by 0.5 g orally 4 times a day to complete 10 days of therapy. This regimen should not be used for pregnant women. The dosage may have to be adjusted if renal function is depressed.

Since optimal therapy for hospitalized patients has not been established, other antibiotics in addition to penicillin are frequently used.

Special considerations. Failure of the patient to improve on the recommended regimens does not indicate the need for stepwise additional antibiotics, but requires clinical reassessment.

The intrauterine device is a risk factor for the development of pelvic inflammatory disease. The effect of removing an intraute-

rine device on the response of acute salpingitis to antimicrobial therapy and on the risk of recurrent salpingitis is unknown.

Adequate treatment of women with acute salpingitis must include examination and appropriate treatment of their sex partners because of their high prevalence of non-symptomatic urethral infection.. Failure to treat sex partners is a major cause of recurrent gonococcal salpingitis.

Follow-up of patients with acute salpingitis is essential during and after treatment. All patients should be recultured for *N. gonorrhoeae* after treatment.

Acute Epididymitis

Acute epididymitis can be caused by *N. gonorrhoeae*, *Chlamydia*, or other organisms. If gonococci are demonstrated by Gram stain or culture of urethral secretions, treatment should be APPG, 4.8 million units, ampicillin, 3.5 g, or amoxicillin, 3.0 g, each with probenecid, 1.0 g. Either regimen is followed by ampicillin, 0.5 g, orally 4 times a day for 10 days; OR

Tetracycline: 0.5 g. orally 4 times a day for 10 days.

If gonococci are not demonstrated, the above tetracycline regimen should be used.

Disseminated Gonococcal Infection

Treatment schedules. There are several, equally effective treatment schedules in the arthritis-dermatitis syndrome. These include the following.

Ampicillin/amoxicillin: ampicillin, 3.5 g, or amoxicillin, 3.0 g, orally, each with probenecid 1.0 g, followed by ampicillin 0.5 g, or amoxicillin, 0.5 g, 4 times a day orally for 7 days; OR

Tetracycline: 0.5 g, orally 4 times a day for 7 days. Tetracycline should not be used for complicated gonococcal infection in pregnant women; OR

Spectinomycin: 2.0 g, intramuscularly twice a day for 3 days (treatment of choice for disseminated infections caused by PPGN); OR

Erythromycin: 0.5 g, orally 4 times a day for 7 days; OR

Aqueous crystalline penicillin G: 10 million units intravenously per day until improvement occurs followed by ampicillin, 0.5 g, 4 times a day, to complete 7 days of antibiotic treatment.

Special considerations. Hospitalization is indicated in patients who may be unreliable, have uncertain diagnosis, or have purulent joint effusions or other complications.

Open drainage of joints other than the hip is not indicated. Intra-articular injection of antibiotics is unnecessary.

Meningitis and endocarditis. Meningitis and endocarditis caused by the gonococcus require high-dose intravenous penicillin therapy. In penicillin-allergic patients with endocarditis, desensitization and administration of penicillin are indicated. Chloramphenicol may be used in penicillin-allergic patients with meningitis.

Gonococcal Infections in Pediatric Patients

With gonococcal infections in children beyond the newborn period, the possibility of sexual abuse must be considered. Genital, anal, and pharyngeal cultures should be obtained from all patients before antibiotic treatment. Appropriate cultures should be obtained from individuals who have had contact with the child.

Prevention of Gonococcal Ophthalmia

When required by state legislation

or indicated by local epidemiologic considerations, effective and acceptable regimens for prophylaxis of neonatal gonococcal ophthalmia include ophthalmic ointment or drops containing tetracycline or erythromycin OR a 1 percent silver nitrate solution.

Special Considerations. Bacitracin is not recommended. The value of irrigation after application of silver nitrate is unknown.

Management of Infants Born to Mothers with Gonococcal Infection

The infant born to a mother with gonorrhea is at high risk of infection and requires treatment with a single intravenous or intramuscular injection of aqueous crystalline penicillin G, 50,000 units to full-term infants or 20,000 units to low-birth-rate infants. Topical prophylaxis for neonatal ophthalmia is not adequate treatment. Clinical illness requires additional treatment.

Neonatal Disease

Gonococcal ophthalmia. Patients should be hospitalized and isolated for 24 hours after initiation of treatment. Untreated gonococcal ophthalmia is highly contagious. Aqueous crystalline penicillin G, 50,000 units/kg/day, in 2 doses intravenously should be administered for 7 days. Saline irrigation of the eyes should be performed as needed. Topical antibiotic preparations alone are not sufficient or required when appropriate systemic antibiotic therapy is given.

Complicated infection. Patients with arthritis and septicemia should be hospitalized and treated with aqueous crystalline penicillin

G, 75,000 to 100,000 units/kg/day, intravenously in 2 or 3 divided doses for 7 days. Meningitis should be treated with aqueous crystalline penicillin G, 100,000 units/kg/day, divided into 3 or 4 intravenous doses, and continued for at least 10 days.

Childhood Disease

Children who weigh 100 lbs (45 kg) or more should receive adult regimens. Children who weigh less than 100 lbs. should be treated as follows.

Uncomplicated disease. Uncomplicated vulvovaginitis, urethritis, proctitis, or pharyngitis can be treated in one visit with amoxicillin, 50 mg/kg, orally with probenecid, 25 mg/kg (maximum 1.0 g), OR with aqueous procaine penicillin G, 100,000 units/kg, intramuscularly plus probenecid, 25 mg/kg (maximum 1.0g).

Special considerations. Topical and/or systemic estrogen therapy are of no benefit in vulvovaginitis. Long-acting penicillins, such as benzathine penicillin G, are not effective. All patients should have follow-up cultures, and the source of infection should be identified, examined, and treated.

Gonococcal ophthalmia. Ophthalmia in children is treated as in neonates, but the dose of penicillin is increased to 100,000 units/kg/day intravenously.

Complicated infections. Patients with peritonitis or arthritis require hospitalization and treatment with aqueous crystalline penicillin G, 100,000 units/kg/day, intravenously for 7 days. Aqueous crystalline penicillin G, 250,000 units/kg/day, intravenously in 6 divi-

ded doses for at least 10 days, is recommended for meningitis.

Allergy to penicillins. Children who are allergic to penicillins should be treated with spectinomycin, 40 mg/kg, intramuscularly. Children older than 8 years may be treated with tetracycline, 40 mg/kg/day, orally in 4 divided doses for 5 days. For treatment of complicated disease, the alternative regimens recommended for adults may be used in appropriate pediatric dosages.

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Bajo esta nueva Sección, todos los compañeros tendrán la oportunidad de enviarnos preguntas médicas de casos difíciles o casos clínicos para opinión experta. Estas preguntas, con sus respuestas, serán publicadas en esta nueva Sección.

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MEDI QUIZ - PARASITOLOGY I

Select One Correct Answer

1. One statement about ascariasis below is incorrect:
 - A. Adults reside in lumen of small bowel
 - B. Infection results from ingestion of eggs which migrate through lungs as vermicules and mature in small bowel after being swallowed
 - C. Heavy infestation may result in bowel obstruction
 - D. Eosinophilia is moderate but constant
 - E. Therapy is with piperazine or bephenium hydroxynaphthoate
2. *Trichuris trichiura*, the whipworm, is a parasitic nematode about which all of the following but one is true:
 - A. Eosinophilia is common
 - B. Infection is established through cutaneous penetration by the pregnant female adult
 - C. Iron deficiency anemia may result from heavy infestation
 - D. Intestinal prolapse is not an unusual complication
 - E. The primary intestinal location of the parasite is the caecum
3. Regarding pinworm infection a nematodal disease, which one of the following statements is incorrect?:
 - A. Caused by *Enterobius vermicularis*
 - B. Eosinophilia occurs frequently
 - C. Pruritis ani is the major symptomatic expression of infection
 - D. Mild leukocytosis and anemia may occur
 - E. Intestinal obstruction usually occurs in the jejunum
4. Each of the following statements about visceral larva migrans is correct, except:
 - A. Human infection usually results from contact with infected pets or their excrement
 - B. Clinical features include fever, hepatomegaly and transient pulmonary infiltrates
 - C. Eosinophilic visceral granulomata and hypergammaglobulinemia are common
 - D. No effective therapy is known but infections are self-limiting
 - E. Isohemagglutinins may be found in sera of infected patients
5. Hookworm infection is characterized by each of the statements below except:
 - A. Iron deficiency anemia is typically the only clinical sequel of infection
 - B. Infective larvae penetrate the skin to infest humans
 - C. Infection is perpetuated by reinfection, adult worms surviving only 2-3 months
 - D. Anemia usually occurs only in menstruating women or growing children
 - E. Size of worm burden can be estimated from the numbers of hookworm eggs/gm of stool
6. Hookworm infection is described incorrectly by one statement below:
 - A. Man is the natural host

- B. *Ancylostoma duodenale* and *Necator americanus* are the infecting nematodes
- C. Pruritis of the skin, edema and erythema are common at the site of penetration of the parasite
- D. High eosinophile counts persist throughout the disease
- E. Diagnosis depends upon identification of the eggs in stools or of the worms after treatment
7. One of the statements about schistosomiasis below is incorrect:
- A. Eosinophile counts are often within normal limits
- B. Miracidia are discharged from parasitized snails and infect man
- C. *Schistosoma haematobium* has a predilection for the urinary bladder
- D. Intestinal schistosomiasis is due to *S. mansoni*
- E. *S. japonicum* eggs are small and have no spine, although there is a small lateral tubercle or hook
8. Enterobiasis is correctly described by all statements below except:
- A. Eosinophilia occurs only during pulmonary migration
- B. Adult worms live free and unattached in the bowel lumen
- C. May precipitate an attack of acute appendicitis
- D. Fomites play a major role in intra-familial infections
- E. Infection is by ingestion of embryonated eggs
9. Factors serving to reduce the incidence of trichinosis in humans include all the following except:
- A. Reduction in per capita consumption of pork
- B. Incorporation of thiabendazole into swine feed
- C. Public awareness of proper methods for cooking pork
- D. Increased use of "ready-to-serve" pork products
- E. Deep-freeze storage of pork products
10. One of the following statements about *Giardia lamblia* is incorrect:
- A. May produce acute colitis in man
- B. Malabsorption with sprue-like stools may occur
- C. Therapy with metronidazole or chloroquine is effective
- D. Diagnosis may be made by small bowel biopsy or by presence of cysts and/or vegetative forms in stools
- E. May invade biliary tree by ascent of common bile duct

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School of Medicine

FRACCION DE EYECCION DEL VENTRI- CULO IZQUIERDO EN PACIENTES CON PRIMER INFARTO TRANSMURAL DEL MIO- CARDIO

Prediman, K., MD et al — Am. J. of Card. Vol. 45 pag. 542-546/80

En este artículo los autores determinaron la fracción de eyección (FE) en las primeras 24 horas en 56 pacientes con su primer infarto del miocardio. La fracción de eyección se determinó mediante el cintilleo múltiple radioactivo. De los 56 pacientes estudiados, 33 pacientes tenían infartos inferiores y 23 tenían infartos anteriores. Los autores encontraron que en 96 de los infartos anteriores tenían fracción de eyección significativamente deprimida. Sin embargo, solo en el 71 por ciento de los infartos inferiores tenían la fracción de eyección significativamente deprimida. Muy importante es que en la mayoría de aquellos pacientes con infartos inferiores y fracción de eyección disminuida, tenían inversión del segmento ST en la pared anterior en ausencia de infartos anteriores. La morbilidad y mortalidad era mucho mayor mientras más disminuida se encontraba la fracción de eyección. En todos aquellos pacientes con la fracción de eyección menor de 30 por ciento la mortalidad era de 100 por ciento, usualmente debido a choque cardiogénico. Los autores concluyen que la fracción de eyección en las primeras 24 horas es un índice excelente para determinar el pronóstico y morbilidad del paciente con su primer infarto transmural. Posiblemente la isquemia de la pared anterior en pacientes con infartos inferiores sea el factor principal relacionado con la disminución de la fracción de eyección en aquellos pacientes con infartos inferiores.

PROTECTIVE EFFECT OF PROSTAGLAN- DIN E₂ IN THE GASTROINTESTINAL TRACT DURING INDOMETHACIN TREAT- MENT OF RHEUMATIC DISEASES

C. Johanson, B. Kollber, R. Nordemar, K. Samuelson, and S. Bergström. Gastroenterology 78: 479-483, 1980.

Las drogas anti-inflamatorias no esteroideas se utilizan con frecuencia en la práctica médica. Los efectos nocivos mayores afectan el tracto gastrointestinal e incluyen aumento de pérdida de sangre en las heces. Experimentos en animales han demostrado que estas drogas pueden causar ulceraciones tanto en el estómago como en el intestino. Prostaglandinas de tipo E₂ (PGE₂) previenen que se desarrollen estas ulceraciones en animales. Johanson et al. reportan en este artículo una evaluación del efecto de PGE₂ oral en pacientes con enfermedades reumáticas tratados con indometacin. El estudio fue de tipo controlado, randomizado, y a doble ciegas. Se midió la pérdida en la excreta de células rojas previamente marcadas con ⁵¹Cr para medir el sangramiento gastrointestinal. Se encontró que indometacin aumentó la pérdida de sangre en las heces de 1 a 2.8 ml. por día ($p < 0.005$). El uso concomitante de PGE₂ redujo el sangramiento a 1.1 ml por día ($p < 0.01$ vs indometacin; sin significancia estadística vs. control) y no interfirió con los efectos beneficiosos de indometacin en la enfermedad reumática. Los hallazgos de este estudio pueden ser de utilidad clínica en el futuro.

Sometido por Angel Olazábal, MD)

EXERCISE FOR POSTCORONARY PATIENTS: AN ASSESSMENT OF INFREQUENT SUPERVISION

Kavanagh T, Shepard RJ, Arch Phys Med Rehab 61: 114-118, 1980.

Un grupo de 49 pacientes que había estado asistiendo a un programa regular de ejercicios semanalmente supervisado por el médico desde un año o más después de haber sufrido un infarto de miocardio, fue transferido a un regimen experimental basado en una prescripción personal de actividad, reforzado por la asistencia cada 8 semanas a la clase de ejercicios médico-supervisada. La data se comparó con las respuestas de 31 pacientes que continuó asistiendo al programa standard de rehabilitación. Diez de los 49 pacientes experimentales demostraron deterioro de su capacidad cardio-respiratoria en el año en curso. De los restantes 39, 23 que ya habían llegado a un "plateau" de entrenamiento mantuvieron su condición, mientras que 16 demostraron ganancias pequeñas continuas de poder aeróbico. El programa infrecuentemente supervisado demostró ser seguro, pero su efectividad terapéutica es dudosa. En lo relativo a pacientes recibiendo tratamiento standard, las ganancias de poder aeróbico fueron pequeñas, y hubo algún deterioro en el electrocardiograma de ejercicio a lo largo del año de estudio.

(Sometido por Rafael Alvarez, MD)

STRATEGIES IN THE TREATMENT OF SYSTEMIC FUNGAL INFECTIONS

G. Medoff and G. S. Kobayashi - New Engl. J. Med. 302: 145, 1980.

Un repaso del uso de agentes antihongos tales como anfotericina B, nystalina, filipina, clotrimazole, miconazole, ketonazole, flucytosina y iodo.

El concepto de combinación de agentes se discute. Una buena lectura y excelente referencia.

(Sometido por Carlos H. Ramírez Ronda, MD)

THE USE OF LETHIUM CARBONATE TO REDUCE INFECTION AND LEUKOPENIA DURING SYSTEMIC CHEMOTHERAPY

Lyman, G. H., et al. New Eng. J. Med. 302: 257, 1980.

El carbonato de litio induce leucocitosis inocua e irreversible en pacientes siquiátricos. Se ha sugerido que el litio puede ser capaz de disminuir la leucopenia asociada con quimioterapia.

Se realizó un estudio de 45 pacientes con carcinoma del pulmón recibiendo quimioterapia. Se le administró a 20 pacientes carbonato de litio 300 mg tres veces al día durante el período de inducción y por 48 hrs post quimioterapia. Los pacientes que recibieron litio tuvieron menos días con neutropenia, menos días con fiebre y neutropenia y menos muertes relacionados a infección.

El carbonato de litio puede que se utilice en el futuro en este tipo de paciente.

(Sometido por Carlos H. Ramírez Ronda, MD)

CHOLERA — A POSSIBLE ENDEMIC FOCUS IN THE UNITED STATES

Blake, P. R., et al - New Engl. J. Med. 302: 305, 1980

Cólera es una infección clásicamente considerada de la región asiática, con una pandemia que comenzó en 1961 y que ha llegado hasta Europa; se ha mantenido fuera del nuevo mundo.

En la región del Golfo de los Estados Unidos

se han descrito 11 casos en donde se recobró *Vibrio Cholerae* O-grupo 1, en personas que comieron canchales. Esto indica que el *Vibrio Cholerae* está presente y persiste en el Golfo de los Estados Unidos.

(Sometido por Carlos H. Ramírez Ronda, MD)

SEXUAL TRANSMISSION OF HEPATITIS A IN HOMOSEXUAL MEN: INCIDENCE AND MECHANISM

Corey, Land K.K. Holmes, *New Eng. J. Med.* 302: 435, 1980.

MEDICAL ASPECTS OF HOMOSEXUALITY EDITORIAL

S. K. Dritz, *New Eng. J. Med.* 302: 463, 1980.

Hepatitis A se añade a otras enfermedades sexualmente transmitidas, tales como hepatitis B, herpes genitalis, uretritis no específica, gonorrea, sífilis, chancroide, tricomoniasis, etc. La incidencia anual de hepatitis A determinada por el desarrollo de anticuerpos fue de 22 por ciento en homosexuales comparados con un grupo de heterosexuales que fue 0.

(Sometido por Carlos H. Ramírez Ronda)

OPTIMAL DIAGNOSIS IN ACUTE MYOCARDIAL INFARCTION, A COST-EFFECTIVENESS STUDY

Grande P, Christiansen C, Podersen A, Christiensen MS - *Circulation* 1980; 61: 723-728

El propósito de este estudio es definir cual prueba diagnóstica es la más eficiente para definir la presencia o ausencia infarto cardíaco agudo.

En el estudio se comparan la kinasa de creatina cardíaca (MB-CK), la aminotransferasa de aspartato, la dehidrogenasa láctica (LDH), la kinasa de creatina total (CK) y el EKG como pruebas diagnósticas en 401 pacientes. La MB-CK fue más específica y sensitiva que las otras pruebas individuales o aún en combinaciones seriadas. Todos los pacientes con infarto agudo tuvieron MB-CK positiva a las 17 horas de admisión. Estiman los autores que con el uso de este método se ahorrarían 1400 días de hospitalización por cada millón de habitantes. Recomiendan ellos que se use la MB-CK en vez de los métodos enzimáticos usuales en el diagnóstico de infarto agudo ya que así se reduce la duración de la hospitalización en los pacientes sin infarto.

(Sometido por Guillermo Cintrón, MD)

APHASIC ADULTS AND THEIR DECISIONS ON DRIVING, AN EVALUATION

Golper LAC, Rau MT, Marshall RC - *Arch Phys Med Rehab.* 61: 34-40, 1980

Este estudio evaluó la propiedad de las decisiones hechas por adultos afásicos para regresar o no a conducir un automóvil después de haber sufrido un accidente cerebrovascular. Se llevó a cabo una comparación entre un grupo de 10 pacientes afásicos que regresaron a conducir un automóvil sin consultar a los profesionales adecuados y un grupo que decidió no volver a conducir. Se encontró que, en base a las destrezas poseídas por estos pacientes, el grupo que volvió a conducir sin ayuda profesional había juzgado adecuadamente su propia capacidad para hacerla. Se concluye que el factor más influyente para tomar la decisión de volver a conducir un automóvil no es en realidad la capacidad presente en el lenguaje.

(Sometido por Jesús A. Maldonado, MD)

FUNCTIONAL CAPACITY EVALUATION, AN EMPIRICAL APPROACH.

Jette AM - Arch Phys Med Rehabil 61: 85-89, 1980.

Se presenta un acercamiento empírico para seleccionar las actividades del diario vivir para evaluar la capacidad funcional de personas no institucionalizadas con incapacidades poliarticulares. Los resultados señalan la posibilidad de reducir la tarea de evaluar estas funciones sin sacrificar lo abarcador de la evaluación. Las 5 categorías funcionales comunes son:

- (1) movilidad física
- (2) transferencias
- (3) tareas domésticas
- (4) tareas de cocina
- (5) cuidado personal

(Sometido por Jesús A. Maldonado, MD)

EXTREMITY AMPUTATION, DISSEMINATED INTRAVASCULAR COAGULATION SYNDROME

Reinstein L, Govindon S - Arch Phys Med, Rehabil. 61: 97-102, 1980

Ha habido reportes ocasionales en la literatura médica de gangrena periférica y subsiguiente amputación de extremidades luego de una infección sistémica. Aunque se ha creído que esto ha ocurrido por embolias sépticas, los estudios patológicos no han revelado este tipo de evidencia. En los pacientes presentados uno requirió una amputación Lisfranc y el otro una transmetatarsiana y ambos tuvieron problemas significativos con la piel y el ajuste de los prótesis. La presencia de una infección viral o bacteriana sistémica aguda, anomalías de la coagulación, tejido patológico indicativo de DIC y lesiones de la piel de las extremidades

que progresan a gangrena seca y requieren amputación bilateral son las características claves de este síndrome.

(Sometido por Jesús A. Maldonado, MD)

REITER'S DISEASE IN WOMEN

David L. Smith, Robert M. Bennett, and Martha G. Regan - Departments of Rheumatology, Providence Medical Center and the University of Oregon Health Sciences Department Arthritis and Rheumatism, Vol. 23, No. 3 (March 1980)

Reiter's disease in its classic form is defined by the triad of arthritis, conjunctivitis, and urethritis and occurs predominantly in men. Recent descriptions have emphasized other ancillary findings: mucocutaneous lesions, plantar fasciitis, Achilles tendinitis, sausage digits, asymmetrical sacroiliitis, and an association with HLA-B27. This study describes 29 women followed over the past 4 years who have a rheumatic disorder most consistent with Reiter's disease. All 29 patients were seronegative, 72 percent presenting with an asymmetrical pauciarticular arthritis, and the majority evidenced lower extremity involvement. During the course of their illness, 52 percent of the patients developed either eye and/or urinary tract involvement. Additional features were mucocutaneous lesions in 8 patients, heel pain or Achilles tendinitis in 15 patients, sausage digit in 20 patients, and clinical sacroiliitis in 20 patients. HLA-B27 was positive in 59 percent of patients, and radiographic bone and joint abnormalities were present in 52 percent of the patients. The recognition of this group of patients has both therapeutic and prognostic implications, because they preferentially respond to indomethacin or phenylbutazone and often pursue a chronic course, albeit without widespread joint destruction.

(Sometido por Edwin Mejías, MD)

CEREBRAL INFARCTION IN YOUNG ADULTS

Bruce D. Snyder, MD and Manuel Ramírez Lassepas, MD - *Stroke* Vol. 11, No. 2, 1980, Pag. 149-153.

Sesenta y un pacientes, entre las edades de 16 a 49 (38 hombres y 23 mujeres), que tuvieron un infarto cerebral, fueron identificados retrospectivamente y categorizados de acuerdo a la etiología probable y la recurrencia del infarto cerebral. Se identificaron 5 grupos. Veintiun pacientes con aterosclerosis prematura se caracterizaron por tener predominancia masculina, frecuencia alta de factores de riesgos, una mortalidad de 23.9 por ciento y una recurrencia para enfermedad cerebrovascular de 41.6 por ciento dentro de una media de un período de seguimiento de 2.4 años. De 7 mujeres en contraceptivos hormonales en el momento del infarto cerebral, una tuvo subsecuentemente un TIA como la única recurrencia durante 2.9 años como la media del período de seguimiento. Siete pacientes con embolia del corazón, se mantuvieron asintomáticos mientras estuvieron en medicación de anticoagulantes: un paciente sufrió un infarto cerebral recurrente cuando se le discontinuó los anticoagulantes, cinco pacientes fueron puestos en una categoría de misceláneos. Estos pacientes tuvieron varias etiologías específicas para sus infartos cerebrales como vasculitis o una embolia. La prognosis varía de acuerdo al tipo de desorden. Trece pacientes no tenían factores etiológicos identificables y no experimentaron mortandad, excepto un episodio de TIA recurrente y otro de infarto cerebral recurrente durante una media de un período de 3 años. Los resultados son descualidos desde el punto de vista del regimen del tratamiento asignado al paciente joven con infarto cerebral.

(Sometido por Rafael Seín, MD)

EXERCISE FOR POSTCORONARY PATIENTS: ASSESSMENT OF INFREQUENT SUPERVISION

Kavanagh, T., Shephard RS - *Arch. Phys. Med. Rehabil.* 61: 114-118, 1980.

A cuarenta y nueve pacientes que participaron regularmente en un programa de ejercicios supervisados por un médico se les transfirió a un programa en que se autosupervisarán, se les re-examinaba cada 8 semanas por un médico del programa regular y se les comparó con 31 que continuaron el programa regular de ejercicios. De ellos 10 se deterioraron en su condición, 23 mantuvieron la condición alcanzada y 16 alcanzaron una pequeña mejoría de su condición aeróbica. El programa con supervisión infrecuente probó ser seguro pero de efectividad dudosa ya que los que ganaron en su condición aeróbica lo hicieron en muy poca escala y hubo, en general, deterioro en el EKG al ejercicio através de un año de estudio.

(Sometido por Frank W. López, MD)

EXTREMELY OBESE PATIENTS: IMPROVEMENTS IN EXCESSIVE TOLERANCE WITH PHYSICAL TRAINING AND WEIGHT LOSS

Foss M. L., Lampman RM, Steingard, DE - *Arch. Phys. Med.* 61: 119-124, 1980

La relación entre el mejoramiento en la tolerancia a ejercicio y el peso fue determinado en 11 pacientes participando a la vez en entrenamiento físico progresivo y restricción calórica como parte de un programa de rehabilitación en residencia. Dos pruebas estandarizadas fueron usadas periódicamente para evaluación cuantitativa de la tolerancia a ejercicios. Se encontró una significativa baja en el peso y un aumento en la tolerancia al ejercicio, con lo se-

gundo ocurrido primero. Se utilizaron programas de intensidad, duración y progresos moderados por ser de este modo más fácilmente tolerados y de mayor seguridad. La mayor aplicabilidad de los resultados de las pruebas estandarizadas está en re-enforzar el progreso de los pacientes en el programa.

(Sometido por Frank W. López, MD)

PRACTICAL CONSIDERATION IN THE REHABILITATION OF THE AGED

T. E. Hunt, MD - *PRCP Journal of the American Geriatrics Society*, Vol XXVIII, No. 2, pag. 59-64.

Un buen cuidado geriátrico provee asistencia al envejeciente para una vida independiente tan larga como sea posible. Es esencial que se le de prioridad a la restauración de las funciones independientes de la persona en coordinación con otras formas de terapia. La rehabilitación médica muchas veces ha sido asociada a metas orientadas hacia el trabajo y hacia metas físicas mayores. La restauración de un parapléjico joven ha sido un modelo de la rehabilitación. El envejeciente también puede ser restaurado a unos niveles óptimos de capacidad funcional conmensurados a sus menores necesidades. Los principios de rehabilitación para el manejo de un impedimento son iguales en la edad avanzada como en cualquier otra edad. Sin embargo hay ciertos factores agregados que influyen profundamente los programas de recuperación en el envejeciente. Estos factores hay que tenerlos en consideración, cuando el médico establece el plan apropiado para el cuidado de sus envejecientes. Una lista de factores es presentada.

Sometido por Rafael Seín, MD)

EXTREMELY OBESE PATIENTS: IMPROVEMENTS IN EXERCISE TOLERANCE WITH PHYSICAL TRAINING AND WEIGHT LOSS

Foss ML, Lampman RM, Schteingart DE - *Arch Phys Med Rehabil* 61: 119-124, March, 1980.

La relación entre el mejoramiento en la tolerancia al ejercicio y el peso fueron determinados para 11 pacientes extremadamente obesos (peso medio = 189 Kg) que concomitantemente participaron en un programa progresivo de ejercicios físicos (caminar-correr) para inducir a la pérdida de peso como parte de un programa de rehabilitación residencial multidisciplinario. Dos pruebas estandarizadas (treadmill mile-walk y graded-exhaustive) se administraron periódicamente para cuantitativamente evaluar el performance. Se observaron reducciones de peso significativos y progreso en la tolerancia al ejercicio, ocurriendo antes lo último mencionado. Coeficientes correlativos entre el peso y medidas de respuesta fisiológicas o performance fueron extremadamente bajos, indicando una respuesta individual diseminadas al entrenamiento y a la probable separación en el entrenamiento y efectos de dieta. Una moderada correlación inversa se encontró entre el peso y la simple medida al performance del trabajo: tiempo de resistencia a la respuesta volicional exhaustiva ($r=0.45$). Los programas de entrenamiento moderados más que de alta intensidad, duración y progresión fueron usados con el grupo de obesos. Estos programas pueden ser administrados sin riesgos y son bien tolerados, pero los terapeutas deben reconocer la inabilidad a predecir mejoría en el performance del ejercicio, en base al peso del paciente. La aplicación mayor de los resultados de la estandarización de las pruebas de ejercicio, reside entonces en el refuerzo directo del progreso del paciente.

(Sometido por Rafael Seín, MD)

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tion-prone individuals or those who might increase dosage; withdrawal symptoms (including convulsions) reported following discontinuation of the drug.

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Precautions: In elderly and debilitated, limit dosage to smallest effective amount to preclude ataxia, oversedation, confusion (no more than 2 capsules/day initially; increase gradually as needed and tolerated). Though generally not recommended, if combination therapy with other psychotropics seems indicated, carefully consider pharmacology of agents, particularly potentiating drugs such as MAO inhibitors, phenothiazines. Observe usual precautions in presence of impaired renal or hepatic function. Paradoxical reactions reported in psychiatric patients. Employ usual precautions in treating anxiety states with evidence of impending depression or suicidal tendencies may be present and protective measures necessary. Variable effects on blood coagulation reported very rarely in patients receiving the drug

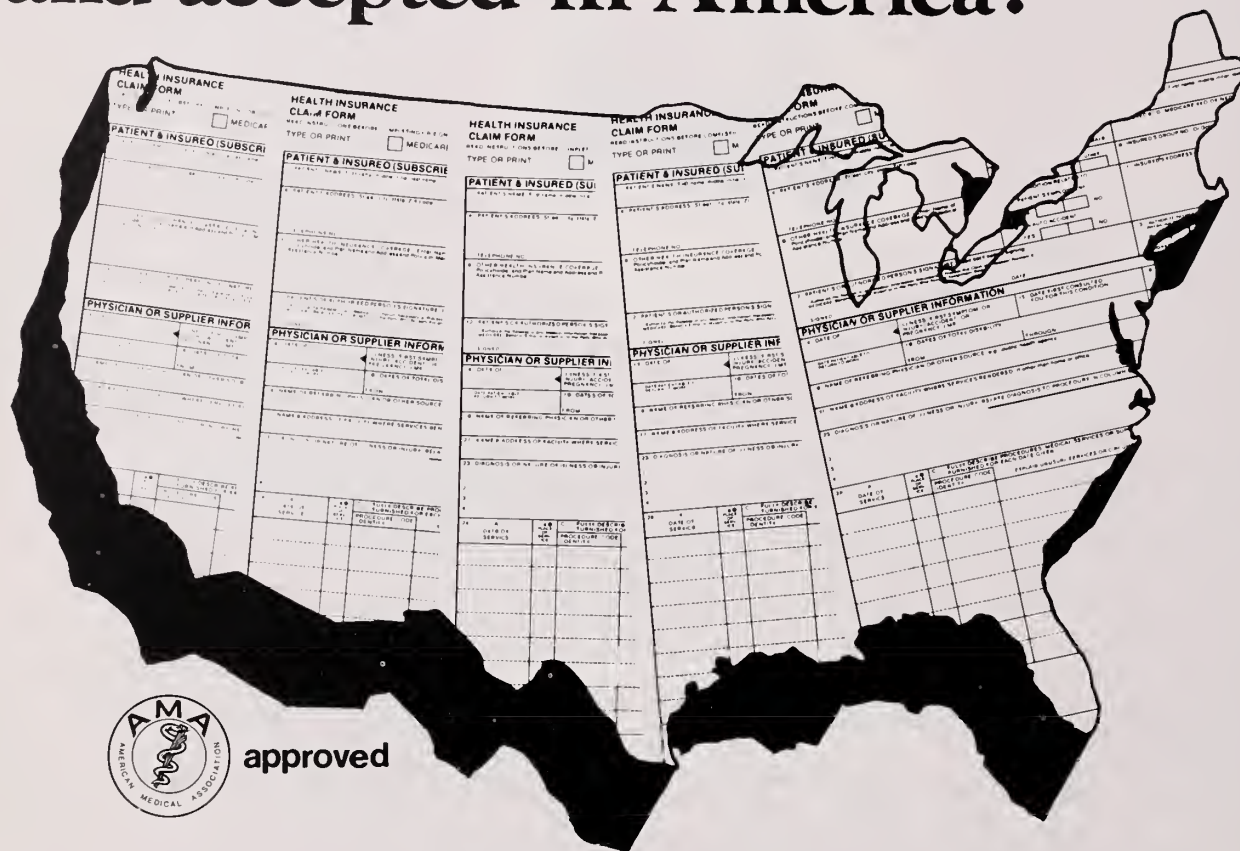
and oral anticoagulants; causal relationship not established.

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MEDI QUIZ – “INFECTIOUS DISEASES”

1. Which of the following chemistry tests performed upon cerebrospinal fluid is helpful in distinguishing bacterial from viral meningitis?
A. Chlo
1. Which of the following chemistry tests performed upon cerebrospinal fluid is helpful in distinguishing bacterial from viral meningitis?
A. Chloride
B. SGOT
C. Lactic acid
D. LDH
2. Which of the following conditions does *not* predispose to pneumococcal sepsis?
A. Sick cell anemia
B. Multiple myeloma
C. Asplenia
D. Chronic granulomatous disease of childhood
3. The *least* common manifestation of adult, acquired toxoplasmosis is:
A. Fever
B. Lymphadenopathy
C. Retinochoroiditis
D. Birth defects in the offspring of infected mothers
4. Which of the following diseases is *not* commonly associated with eosinophilia?
A. Amebiasis
B. Trichinosis
C. Ascariasis
D. Strongyloidiasis
E. Schistosomiasis
5. Which of the following diseases can result in anergy to delayed hypersensitivity skin testing?
A. Measles
B. Infectious mononucleosis
C. Sarcoidosis
D. Hodgkin's disease
E. All of the above
6. Effective prophylaxis for “travelers’ diarrhea” has been achieved with daily administration of low-dose:
A. Ampicillin
B. Sulfonamides
C. Doxycycline
D. Erythromycin
E. None of the above
7. A known intravenous drug abuser presents with fever, heart murmur, and chest x-ray evidence of a septic embolus. Initial therapy should always include:
A. Heparin
B. A penicillinase-resistant penicillin
C. Penicillin G plus an aminoglycoside
D. Carbenicillin plus an aminoglycoside
E. None of the above
8. A patient who is found to have septicemia due to *Streptococcus bovis* should have:
A. Six weeks of therapy with a penicillin plus an aminoglycoside.
B. A work-up for an underlying immune disorder
C. Therapy for the acute septicemia only
D. A complete work-up for a gastrointestinal malignancy

- E. A complete work-up for urinary tract obstruction
9. The majority of cases of post-transfusion hepatitis can be attributed to:
- Hepatitis B virus
 - Hepatitis A virus
 - Cytomegalovirus
 - Epstein-Barr virus
 - Non-A, non-B hepatitis agent
10. With regard to group A streptococcal skin and mucous membrane infections:
- Prompt, adequate treatment with penicillin significantly reduces the incidence of acute post-streptococcal glomerulonephritis
 - Prompt adequate treatment with penicillin significantly reduces the incidence of acute rheumatic fever following streptococcal pharyngitis
 - The ASO titer is the most reliable serologic test for diagnosing impetigo
 - Penicillin-resistant strains of streptococcus are becoming a problem in some geographic areas
11. Which of the following statements is *not* true concerning pneumonia due to the organism *Pneumocystis carinii*?
- Incidence in this country is almost entirely limited to severely immunocompromised patients
 - Routine sputum cultures or bronchial washings usually establish the diagnosis
 - Effective prophylaxis with trimethoprim-sulfamethoxazole has been demonstrated in children undergoing therapy for hematologic malignancies
 - The clinical syndrome is character-
- ized by fever, non-productive cough, severe tachypnea and cyanosis, and a mortality that approaches 100 per cent in untreated cases.
12. Three days following a mild influenzalike illness, an 8-year-old boy develops intractable vomiting, severe headache, and declining mental status over a two-day period. On examination, he is noted to be obtunded, with papilledema but no nuchal rigidity. In addition to routine laboratory tests, which of the following should be performed immediately?
- Serum glucose, SGOT, bilirubin, and prothrombin time
 - Emergency barium swallow
 - Emergency lumbar puncture
 - Only close observation and symptomatic therapy for 24 hours, and then reassess the patient
13. Which of the following is *not* true concerning antibiotic-induced pseudomembranous enterocolitis?
- Recent human to animal studies suggest many, if not all, cases can be attributed to colonic overgrowth of the toxin-producing organism *Clostridium difficile*
 - Oral vancomycin is effective in reducing or abolishing the manifestations of this disorder
 - Only the antibiotic clindamycin has been shown to produce this clinical syndrome
 - Clinically, the diagnosis is made by sigmoidoscopy
14. Which of the following clinical manifestations can occur with *Mycoplasma pneumoniae* infections?
- Hemolysis due to cold-reacting anti-

bodies

- B. Otitis media
- C. Raynaud's phenomenon
- D. Meningitis
- E. All of the above

15. Penicillin resistance due to penicillinase production has been demonstrated in

all of the following organisms *except*:

- A. *Streptococcus pneumoniae* (pneumococcus)
- B. *Staphylococcus aureus*
- C. *Hemophilus influenzae*
- D. *Neisseria gonorrhoeae* (gonococcus)

REPRINTED BY PERMISSION FROM HOSPITAL PHYSICIAN VOL. 15, NO. 12. THE INFECTIOUS DISEASES QUIZ WAS PREPARED BY J. WILLIS HURST, MD AND J. BOYD FRANCIS, MD

(Contestaciones en página 248)

Las siguientes preguntas fueron sometidas a la Junta Editora por lectores de nuestro Boletín:

¿CUALES SON LAS INDICACIONES ACTUALES PARA EL USO DE CIMETIDINA? FAVOR COMENTAR SOBRE SU MECANISMO DE ACCION.

La agencia Federal Drug Administration aprobó el uso de cimetidina en pacientes con úlceras duodenales y con estados de hipersecreción gástrica como el síndrome de Zollinger - Ellison.

Cimetidina es un agente que bloquea algunas de las acciones de histamina. Específicamente, cimetidina antagoniza la acción de histamina mediada por receptores histamínicos de tipo dos.

Los anti-histamínicos convencionales antagonizan la acción de histamina en el músculo liso del corazón y de los bronquios y que es mediado por receptores de histamina de tipo uno, pero no bloquean la estimulación de secreción gástrica que es mediada por receptores de tipo dos.

Cimetidina inhibe la estimulación de secreción gástrica inducida por histamina. Interesantemente, cimetidina también inhibe la secreción gástrica estimulada por gastrina, insulina, cafeína y comida.

Los efectos secundarios de cimetidina son varios. Leves anormalidades en la concentración de creatinina y transaminasas hepáticas ocurren ocasionalmente, pero la disfunción renal y hepática parece ser mínima. Agrandecimiento del pecho usualmente leve y temporero ha ocurrido en cerca del 4 por ciento de los pacientes con el síndrome de Zollinger - Ellison y en cerca de un 2 por ciento de los pacientes con úlceras y tratados por tres meses o más. Granulocitopenia al igual que trombocitopenia y anemia ocurrieron con relativa frecuencia con la droga metiamida que precedió el desarrollo de cimetidina. La composición química de cimetidina sin embargo, es diferente y granulocitopenia se estima que puede ocurrir en uno de cada 100,000 cursos de terapia y la probabilidad de desarrollar anemia aplásica en uno en tres millones.

Varios casos de confusión mental asociado con cimetidina se han reportado. Estos han sido usualmente en pacientes de edad avanzada y/o pacientes con enfermedad moderada a severa hepática y renal. Prolongación del tiempo de protrombina en pacientes en anti-coagulantes orales también se ha reportado.

Referencia

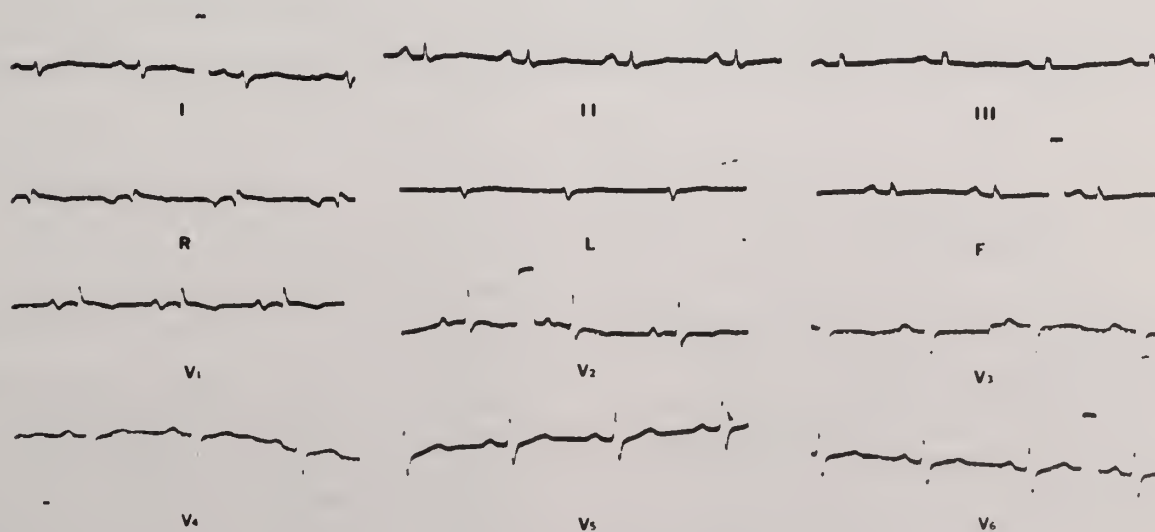
Third Symposium on Histamine H₂ - Receptor Antagonists: Clinical Results with Cimetidine. Gastroenterology 74: 388-488, 1978.

ELECTROCARDIOGRAM OF THE MONTH

The electrocardiogram (ECG), Figure 1, was performed (4-15-74) on a 36-year-old female with multiple hospital admissions for chest and abdominal pains and severe congestive heart failure. Schistosomiasis had been diagnosed in the past (positive circumoval test and rectal biopsy). The blood pressure was 70/50 mm Hg. S₂ was loud in the pulmonic area. Serum albumin was 2.3 g per cent. Silent mitral stenosis was considered. Temporary loss of consciousness occurred. A chest x-ray, lung and heart scans revealed pleural but no pericardial fluid. On 4-28-74, she became cyanotic and unresponsive, without pulse or blood pressure. CVP's were 29 and 35 cm of water. She improved slowly, but anisocoria was noted. A low cardiac output syndrome was considered likely. Surgery was performed on 4-30-74, and was tolerated well. The CVP decreased to 14 cm. Early postoperatively she developed dyspnea and restlessness. Cardiac arrest ensued and she expired.

DIAGNOSIS:

1. *Describe the pertinent electrocardiographi features.*
2. *What morphological diagnoses can be derived from the ECG?*
3. *What is your clinical diagnosis correlating all the data?*
4. *Explain the pathogenesis of this unusual apparition.*



ANSWER

The ECG shows a normal sinus rhythm and a QRS axis of + 105-110 degrees. A qR complex is present in lead V₁ and a R/S (ratio < 1) in V₆; small q waves are seen in V₂₋₃ but no q appears in V₅₋₆. The QRS voltage is low, in general. The P waves are slightly broad and notched in lead II and diphasic in V₁. The trace suggests right ventricular hypertrophy (RVH) and left atrial enlargement as seen in mitral stenosis. Cardiac catheterization suggested constrictive pericarditis or restrictive cardiomyopathy.

At surgery, constrictive pericarditis was found. The pericardium was 5 mm thick. Pericardiectomy was performed. Autopsy revealed a pulmonary embolus in the right pulmonary artery and pericardial constriction. The left ventricle (LV) was small; the right atrium was dilated and hypertrophied and the left atrium was dilated; the right ventricle (RV) was hypertrophied (5 mm thick); there was no pulmonary evidence of schistosomiasis.

Several conditions other than RVH (T waves are usually inverted in V₁) can exhibit prominent R waves in the right precordial leads, such as: a normal variant (seen in obesity, the axis may be normal in the frontal plane), right bundle branch block (T usually inverted in V₁), dorsal, high true posterior (T usually tall and symmetrical in V₁; associated with inferior or lateral infarction) - and posterolateral myocardial infarctions, hypertrophic obstructive cardiomyopathy, Duchenne muscular dystrophy, Type A Wolff-Parkinson-White syndrome, mirror-image dextrocardia, annular subvalvular mitral aneurysm and Wilson's central terminal error. Right axis deviation (RAD) and a RVH pattern have been encountered infrequently in constrictive pericarditis, associated with annular pericardial and subpulmonic constriction. Heavy basal fibrosis leading to cardiac distortion and rotation with a change of direction of the electrical forces could produce a pattern mimicking RVH. The vertical or RAD may be due to RV injury and strain, and disuse atrophy of an underloaded LV. The P waves may be wide, notched and bifid (31-80 percent of cases) with a taller second peak resembling P mitrale, due to delayed or aberrant conduction in the atria, Bachman's bundle, atrial hypertension, dilatation and hypertrophy. Other findings in constrictive pericarditis are low QRS voltage, ST-T wave abnormalities, abnormal Q waves, QRS slurring, atrial fibrillation (about 30 percent) and occasionally atrial flutter. An echocardiogram would probably have been of diagnostic help.

Charles D. Johnson, MD

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2. Ha D, Kraft DI, Stein PD: The anteriorly oriented horizontal vector loop: The problem of distinction between direct posterior myocardial infarction and normal variant. *Am Heart J* 88: 408, 1974.
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5. Orlando J, Aronow WS: Value of the vectorcardiogram in assessing tall R waves in right precordial leads. *Chest* 69: 540, 1976.
6. Schnittger I, et al: Echocardiography: Pericardial thickening and constrictive pericarditis. *Am J Cardiol* 42: 388, 1978.
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8. Surawicz B: Assessing abnormal ECG patterns in the absence of heart disease. *Cardiovasc Med* 2: 629, 1977.
9. Voelkel AG, et al: Echocardiographic features of constrictive pericarditis. *Circulation* 58: 871, 1978.

PEDIATRIC DERMATOLOGY SEMINAR VIII —
Preliminary Notice

The 8th Annual Pediatric Dermatology Seminar will convene at the Eden Roc Hotel, Miami Beach, Florida, February 26 - March 1, 1981. It will be followed by a twelve day post-seminar tour to Tahiti and New Zealand with an optional extension to Australia.

For information, contact: Guinter Kahn, MD, 16800 N. W. 2nd Ave., Miami, Florida 33169. (305-652-8600).

NEWS FROM THE AMERICAN COLLEGE OF SURGEONS

Postgraduate Courses
66th Annual Clinical Congress
Atlanta, October 19-24, 1980

1. Pre-and Postoperative Care of the Critically Ill Patient - C. James Carrico, MD, FACS, Chairman
Tuesday - Friday, 8:30 a.m.- 12:00 noon
Tuesday - Thursday, Room A, Georgia World Congress Center
Friday, Auditorium, Georgia World Congress Center
2. Gastrointestinal Disease - Larry C. Carey, MD, FACS, Chairman
Monday - Wednesday, 1:30 p.m - 5:00 p.m.
Thursday, 1:00 p.m. - 3:00 p.m.
Room 102, Georgia World Congress Center
3. Diseases of the Liver, Biliary Tract and Pancreas - Robert Zeppa, MD, FACS, Chairman

- Tuesday - Friday, 8:30 a.m. - 12:00 noon
Room 102, Georgia World Congress Center
4. Cardiac Surgery - Vallee L. Willman, MD, FACS, Chairman
Tuesday - Friday, 8:30 a.m.- 12:00 noon
Liberty Hall, Omni International Hotel
5. Trauma: Systems Support in the Critically Injured - Peter C. Canizaro, MD, FACS, Chairman
Tuesday - Friday, 8:30 a.m. - 12:00 noon
Ballroom East, Atlanta Hilton Hotel
6. Gynecology and Obstetrics: Surgical Techniques and Management of Intraoperative Complications - James L. Breen, MD, FACS, Chairman
Monday - Tuesday, 1:30 p.m. - 5:00 p.m.
Room 309, Georgia World Congress Center
7. Fractures of the Tibia - Lewis D. Anderson, MD, FACS, Chairman
Tuesday - Wednesday, 1:30 p.m. - 5:00 p.m.
Room 209, Georgia World Congress Center
8. Thoracic Surgery - Benson B. Roe, MD, FACS, Chairman
Monday - Wednesday, 1:30 p.m. - 5:00 p.m.
Thursday, 1:00 p.m. - 3:00 p.m.
Liberty Hall, Omni International Hotel
9. Endocrine Aspects of Pediatric Surgery - John D. Burrington, MD, FRCS (C), FACS, Chairman
Tuesday - Wednesday, 8:30 a.m. - 12:00 n.
Room 204, Georgia World Congress Center
10. Current Controversies in Cancer - Edward F. Scanlon, MD, FACS, Chairman; Charles M. McBride, MD, FACS, Vice Chairman

Tuesday - Friday, 8:30 a.m. - 12:00 noon
 Mimosa Hall, Omni International Hotel

11. Urologic Surgery - Abraham T. K. Cockett, MD, FACS, Chairman
 Tuesday - Wednesday, 8:30 a.m.-12:00 noon
 Room 301, Georgia World Congress Center

12. Colon and Rectal Surgery - Gerald Marks, MD, FACS, Chairman
 Wednesday, 1:30 p.m. - 5:00 p.m.
 Thursday, 8:30 a.m. - 12:00 noon
 Room 100, Georgia World Congress Center

13. Plastic and Maxillofacial Surgery: The Nose: Congenital Deformities, Physiology and Deformities after Trauma and Cancer Surgery - William C. Grabb, MD, FACS, Chairman
 Tuesday - Wednesday, 1:30 p.m - 5:00 p.m.
 Room 300, Georgia World Congress Center

14. Rehabilitative Measures Available for Use by the Head and Neck Surgeon - Byron J. Bailey, MD, FACS, Chairman
 Tuesday - Wednesday, 8:30 a.m.-12:00 noon
 Room 210, Georgia World Congress Center

15. Ophthalmic Surgery: Update of Pediatric Surgery - William H. Jarrett II, MD, FACS, Chairman
 Tuesday - 8:30 a.m. - 12:00 noon; 1:30 p.m. 5:00 p.m.
 Wednesday, 8:30 a.m. - 12:00 noon
 Room 302, Georgia World Congress Center

16. Basic Science Problems in Surgery: Gastrointestinal Physiology - David Fromm, MD, FACS, Chairman
 Tuesday - Wednesday, 8:30 a.m. - 12:00 n
 Room 100, Georgia World Congress Center

17. Peripheral Vascular Surgery - W. Andrew Dale, MD, FACS, Chairman
 Monday - Wednesday, 1:30 p.m. - 5:00 p.m.
 Room A, Georgia World Congress Center

18. Management of Head Injuries, including Moni-

toring and Problems of Cerebral Perfusion and Oxygenation - Donald P. Becker, MD, FACS, Chairman

Monday - Tuesday, 1:30 p.m. - 5:00 p.m.
 Room 308, Georgia World Congress Center

Specialty Sessions
 66th Annual Clinical Congress
 Atlanta, October 19-24, 1980

Colon and Rectal Surgery

Friday, October 24, Hyatt Regency Atlanta Hotel

Panel: ADVANCES IN ANORECTAL SURGERY
 8:30 a.m. - 10:00 a.m. - Richard M. Alexander, MD, FACS, Moderator

Panel: KOCK PROCEDURE UPDATE
 10:30 a.m. - 12:00 noon - Robert J. Rubin, MD, FACS, Moderator

Panel: CURRENT MANAGEMENT OF DIVERTICULITIS
 1:30 p.m. - 3:00 p.m. Stanley M. Goldberg, MD, FACS, Moderator

Panel: COLONOSCOPY FOR SURGEONS
 3:30 p.m. - 5:00 p. m. - J. Byron Gathright, Jr., MD, FACS, Moderator

Gynecology and Obstetrics

Monday, October 20, Georgia World Congress Center

Panel: TREATMENT OF MALIGNANCY DURING PREGNANCY
 8:30 a.m. - 10:00 a.m. - John L. Lewis, Jr., MD, FACS, Moderator

Panel: NEW TECHNIQUES IN THE DIAGNOSIS OF GYNECOLOGIC MALIGNANCY
 10:30 a.m. - 12:00 noon - Hervy E. Averette, MD, FACS, Moderator

Tuesday, October 21

Symposium: RECONSTRUCTIVE VAGINAL SURGERY AND FEMALE UROLOGIC PROBLEMS

9:00 a.m. - 12:00 noon - Joseph H. Pratt, MD, FACS,
Presiding Officer

Wednesday, October 22

Panel: TREATMENT OF DYSFUNCTIONAL UTERINE BLEEDING

8:30 a.m. - 10:00 a.m. - A. Brian Little, MD, CM,
FRCS (C), FACS

Panel: THROMBO-EMBOLIC DISEASE IN GYNECOLOGY AND OBSTETRICS

10:30 a.m. - 12:00 noon - Philip J. Krupp, Jr., MD,
FACS, Moderator

Thursday, October 23

Panel: DIAGNOSIS AND TREATMENT OF PELVIC INFECTIONS

8:30 a.m. - 10:00 a.m. - Robert E. Rogers, MD, FACS,
Moderator

Panel: MEDICAL LEGAL ASPECTS OF GYNECOLOGIC SURGERY

10:30 a.m. - 12:00 noon - Edward A. Banner, MD,
FACS, Moderator

Neurological Surgery

Monday, October 20, Georgia World Congress Center

Interdisciplinary Symposium: THE PARALYZED FACE

9:00 a.m. - 12:00 noon

Theodore Kurze, MD, FACS, Co-Presiding Officer
Mansfield F. W. Smith, MD, FACS, Co-Presiding Officer

Tuesday, October 21

Panel: PULMONARY EMBOLISM IN NEUROSURGERY

8:30 a.m. - 10:00 a.m. - Raeburn C. Llewellyn, MD,
FACS, Moderator

Panel: CAROTID ARTERY INJURIES

10:30 a.m. - 12:00 noon - Glenn W. Kindt, MD, FACS,
Moderator

Ophthalmology

Monday, October 20, Georgia World Congress Center

Interdisciplinary Symposium: SURGERY OF NEURO-OPHTHALMOLOGIC PROBLEMS

1:30 p.m. - 4:30 p.m.

Harrison D. Cavanagh, MD, FACS, Presiding Officer

Orthopaedic Surgery

Tuesday, October 21, Georgia World Congress Center

Symposium: PATELLOFEMORAL INSTABILITY

9:00 a.m. - 12:00 noon - Jack C. Hughston, MD, FACS,
Presiding Officer

Wednesday, October 22

Panel: WRIST INJURIES - A FRESH LOOK

8:30 a.m. - 10:00 a.m. - Richard S. Bryan, MD, FACS,
Moderator

Panel: CHRONIC PAIN - LOW BACK AND EXTREMITIES

10:30 a.m. - 12:00 noon - Edward H. Simmons, MD,
FRCS (C), FACS

Otorhinolaryngology

Monday, October 20, Georgia World Congress Center

Interdisciplinary Panel: NEWER DIAGNOSTIC MODALITIES AVAILABLE TO THE HEAD AND NECK SURGEON

1:30 p.m. - 3:00 p.m. - Paul H. Ward, MD, FACS, Moderator

Interdisciplinary Panel: ADJUNCTIVE PROCEDURES USED IN HEAD AND NECK AESTHETIC AND RECONSTRUCTIVE SURGERY

3:30 p.m. - 5:00 p.m. - E. Gaylon McCollough, MD,
FACS, Moderator

Wednesday, October 22

Interdisciplinary Panel: HEAD AND NECK CONDITIONS AFFECTING THE DEVELOPMENT OF HEARING AND COMMUNICATIVE SKILLS

1:30 p.m. - 3:00 p.m. - Bobby R. Alford, MD, FACS, Moderator

Interdisciplinary Panel: MANAGEMENT OF ACUTE UPPER AIRWAY OBSTRUCTION IN CHILDREN

3:30 p.m. - 5:00 p.m. - Gabriel F. Tucker, Jr., MD, FACS, Moderator

Thursday, October 23

Interdisciplinary Panel: HEADACHE AND FACIAL PAIN - DIAGNOSTIC MEASURES AND SURGICAL TREATMENT MODALITIES

8:30 a.m. - 10:00 a.m. - Werner D. Chasin, MD, FACS, Moderator

Interdisciplinary Panel: NEW DEVELOPMENTS IN FLAPS USED IN HEAD AND NECK RECONSTRUCTIONS

10:30 a.m. - 12:00 noon - Charles J. Krause, MD, FACS, Moderator

Pediatric Surgery

Monday, October 20, Georgia World Congress Center

Panel: UPDATE OF SPECIAL PEDIATRIC SURGERY PROBLEMS

1:30 p.m.- 3:00 p.m. James L. Talbert, MD, FACS, Moderator

Plastic and Maxillofacial Surgery

Tuesday, October 21, Georgia World Congress Center

Interdisciplinary Symposium: CRANIOFACIAL SURGERY: EVALUATION AND RESULTS

9:00 a.m. - 12:00 Noon - Joseph E. Murray, MD, FACS, Presiding Officer

Thursday, October 23

Interdisciplinary Panel: CHEST WALL AND BREAST RECONSTRUCTION

8:30 a.m. - 10:00 a.m. Maurice J. Jurkiewicz, MD, FACS, Moderator

Interdisciplinary Panel: VASCULAR ANOMALIES OF THE EXTREMITIES

10:30 a.m. - 12:00 noon - J. William Futrell, MD, FACS, Moderator

Panel Co-Sponsored with the Advisory Council for General Surgery: HEAD AND NECK CANCER: UPDATE ON RECONSTRUCTIVE TECHNIQUES

1:30 p.m. - 3:00 p.m. - Milton T. Edgerton, Jr., MD, FACS, Co-Moderator and William A. Maddox, MD, FACS, Co-Moderator

Thoracic Surgery

Friday, October 24, Atlanta Hilton Hotel

Symposium: CHALLENGES OF THE MEDIASTINUM

9:00 a.m. - 12:00 noon - Philip E. Bernatz, MD, FACS, Presiding Officer

Panel: PULMONARY FUNCTION - ASSESSMENT AND PRESERVATION

1:30 p.m. - 3:00 p.m. - Richard M. Peters, MD, FACS, Moderator

Panel: EMPYEMA AND PLEURAL SPACE PROBLEMS
3:30 p.m. - 5:00 p.m.- Francis Robicsek, MD, FACS, Moderator

Urologic Surgery

Tuesday, October 21, Georgia World Congress Center

Panel: TESTIS NEOPLASMS: DIAGNOSIS AND STAGING; SURGERY; CHEMOTHERAPY AND FOLLOWUP STUDY

1:30 p.m. - 3:00 p.m. - John P. Donohue, MD, FACS, Moderator

Interdisciplinary Panel: HYPOSPADIAS UPDATE, 1980

3:30 p.m. - 5:00 p.m. - George E. Hurt, Jr., MD, FACS, Moderator

Thursday, October 23

Interdisciplinary Panel: MONITORING THE SERIOUSLY ILL UROLOGY PATIENT

8:30 a.m. - 10:00 a.m. - Anton J. Bueschen, MD, FACS, Moderator

Interdisciplinary Panel: URODYNAMICS: USE AND ABUSE

10:30 a.m. - 12:00 noon - Carl A. Olsson, MD, FACS, Moderator

Lectures
66th Annual Clinical Congress
Atlanta, October 19-24, 1980

The following lectures will be given in Room C of the Georgia World Congress Center, except for the Scudder Oration on Trauma, which will be presented in Room 100, Georgia World Congress Center.

1. AMERICAN UROLOGICAL ASSOCIATION LECTURE

Lecturer to be announced.

Monday, October 20, 10:15 a.m. - 11:15 a.m.

2. JOHN H. GIBBON, JR. LECTURE

Norman E. Shumway, MD, FACS, Professor and Chairman of the Department of Surgery, Stanford University, Stanford.

Monday, October 20, 3:30 p.m. - 4:30 p.m.

3. SCUDDER ORATION ON TRAUMA

Francis D. Moore, MD, FACS, Elliott Carr Cutler Professor of Surgery, Harvard University, Boston.

Tuesday, October 21, 1:30 p.m. - 2:15 p.m.

4. I. S. RAVDIN LECTURE IN THE BASIC SCIENCES
RADIOIMMUNOASSAY IN CLINICAL MEDICINE

Rosalyn S. Yalow, PhD, Chairman, Department of Clinical Sciences, Montefiore Hospital and Medical Center, Bronx.

Wednesday, October 22, 1:30 p.m. - 2:15 p.m.

5. MARTIN MEMORIAL LECTURE

Alton Ochsner, MD, FACS, Professor Emeritus, Tulane University, New Orleans

Thursday, October 23, 3:15 p.m. - 3:55 p.m.

General Sessions
66th Annual Clinical Congress
Atlanta, October 19-24, 1980

1. OPENING CEREMONY

William H. Muller, Jr., MD, FACS, Presiding
Peter D. Olch, MD, Speaker

Monday, October 20, 9:30 a.m. - 10:00 a.m.

2. OPERATING ROOM ENVIRONMENT PANEL
OPERATING ROOM DESIGN AND MANAGEMENT: THE ART AND SCIENCE

Gerald Klebanoff, MD, FACS, Moderator

Monday, October 20, 10:15 a.m. - 12:15 p.m.

3. MEDICAL DEVICES PANEL: PROSTHESES FOR VASCULAR REPLACEMENT

Lester R. Sauvage, MD, FACS, Moderator

Monday, October 20, 10:30 a.m. - 12:00 Noon

4. THE CURRENT ROLE OF PROPHYLACTIC ANTIBIOTICS IN SURGICAL PATIENTS

Robert E. Condon, MD, FACS, Moderator

Monday, October 20, 1:30 p.m. - 3:00 p.m.

5. INTERNATIONAL RELATIONS PANEL: CLINICAL SURGICAL RESEARCH - A WORLD-WIDE PERSPECTIVE

James B. D. Mark, MD, FACS, Moderator

- Monday, October 20, 1:30 p.m. - 3:30 p.m.
6. NEW APPROACHES IN THE DIAGNOSIS AND MANAGEMENT OF THE ACUTE ABDOMEN
- John M. Beal, MD, FACS, Moderator
Tuesday, October 21, 8:30 a.m. - 10:00 a.m.
7. CURRENT PROBLEMS IN THE MANAGEMENT OF CANCER OF THE LUNG
- Donald L. Paulson, MD, FACS, Moderator
Tuesday, October 21, 10:30 a.m. - 12:00 noon
8. PAPERS SESSION I
- Moderator to be announced.
Tuesday, October 21, 1:30 p.m. - 4:30 p.m.
9. FORUM FOR GENERAL SURGERY PROGRAM DIRECTORS
- Robert E. Hermann, MD, FACS, Moderator
Tuesday, October 21, 1:30 p.m. - 3:30 p.m.
10. PRE- AND POSTOPERATIVE CARE PANEL: EVALUATION AND PRESERVATION OF RENAL FUNCTION
- Joseph M. Civetta, MD, FACS, Moderator
Tuesday, October 21, 1:30 p.m. - 3:00 p.m.
11. TRAUMA SYMPOSIUM: NUTRITION IN TRAUMA
- Charles F. Frey, MD, FACS, Presiding Officer
Tuesday, October 21, 2:30 p.m. - 5:00 p.m.
12. MANAGEMENT OF FLUID AND ELECTROLYTE BALANCE IN THE SEVERELY ILL SURGICAL PATIENT
- G. Thomas Shires, MD, FACS, Moderator
Tuesday, October 21, 3:30 p.m. - 5:00 p.m.
13. INFLAMMATORY DISEASE OF THE INTESTINE
- Oliver H. Beahrs, MD, FACS, Moderator
Wednesday, October 22, 8:30 a.m. - 10:00 a.m.
14. PANEL SPONSORED BY THE COMMITTEE TO STUDY RELATIONSHIPS WITH YOUNG SURGEONS
FEDERAL REGULATION: IMPLICATIONS FOR SURGICAL PRACTICE
- C. Rollins Hanlon, MD, FACS, Moderator
Wednesday, October 22, 10:30 a.m. - 12:00 noon
15. CORRELATIVE CLINIC
- Edward L. Bradley, III, MD, FACS, Case Moderator
H. Harlan Stone, MD, FACS, Case Moderator
Wednesday, October 22, 1:30 p.m. - 3:30 p.m.
16. CANCER SYMPOSIUM: UPDATE ON BREAST CANCER
- Guy F. Robbins, MD, FACS, Presiding Officer
Wednesday, October 22, 2:30 p.m. - 5:00 p.m.
17. SURGICAL MANAGEMENT OF PATIENTS WITH COAGULATION DEFECTS
- F. William Blaisdell, MD, FACS, Moderator
Thursday, October 23, 10:30 a.m. - 12:00 noon
18. SURGICAL EDUCATION IN MEDICAL SCHOOLS PANEL: SURGICAL INVOLVEMENT IN THE TEACHING OF BASIC SCIENCE
- Arthur H. Aufses, Jr., MD, FACS, Moderator
Thursday, October 23, 10:30 a.m. - 12:00 Noon
19. PAPERS SESSION II
- Moderator to be announced.
Thursday, October 23, 1:00 p.m. - 3:00 p.m.

20. TRAUMA ACTION PROGRAM: EDUCATION
OF THE SURGEON IN TRAUMA

Donald D. Trunkey, MD, FACS, Moderator
Thursday, October 23, 1:00p.m. - 3:00 p.m.

21. WHAT'S NEW IN SURGERY?

Frank G. Moody, MD, FACS, Presiding Officer
Friday, October 24, 8:30 a.m. - 12:00 noon

"It hurts when I do this."



In diagnosing work-related musculoskeletal disorders, such as low back pain, it is often helpful to have the patient simulate the motions he does at work.

Dual-acting **PARAFON FORTE** (chlorzoxazone 250 mg plus acetaminophen 300 mg) tablets

promptly relieves both pain and spasm*

In acute musculoskeletal conditions,*
PARAFON FORTE tablets are:

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combining the effective pain relief^{1,2} and safety³⁻⁵ of **TYLENOL**® acetaminophen and the muscle-spasm reduction of chlorzoxazone

Prompt-acting

clinical studies have shown that patients respond by the first evaluation period (day 2)^{6,7}

Minimally sedating

clinical studies have shown that most patients remain mentally alert when the drug is administered at recommended doses^{7,8}

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DEPOT STOCKED 500's:
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Summary of Prescribing Information

***Indications:** Based on a review of this drug by the National Academy of Sciences-National Research Council and/or other information, FDA has classified the indications as follows:
"Probably" effective as an adjunct to rest and physical therapy for the relief of discomfort associated with acute, painful musculoskeletal conditions. The mode of action of this drug has not been clearly identified, but may be related to its sedative properties. Chlorzoxazone does not directly relax tense skeletal muscles in man.

Contraindications: Sensitivity to either component.

Warnings: Usage in Pregnancy—Use in women of childbearing potential only when potential benefits outweigh possible risks.

Precautions: Exercise caution in patients with known allergies or history of drug allergies. If a sensitivity reaction or any signs or symptoms suggestive of liver dysfunction are observed, the drug should be stopped.

Adverse Reactions: Occasionally, drowsiness, dizziness, light-headedness, malaise, overstimulation or gastrointestinal disturbances may be noted; rarely, allergic-type skin rashes, petechiae, ecchymoses, angioneurotic edema or anaphylactic reactions. In rare instances, chlorzoxazone may possibly have been associated with gastrointestinal bleeding. While **PARAFLEX**® (chlorzoxazone) tablets and other chlorzoxazone-containing products have been suspected as being the cause of hepatic toxicity in approximately twenty-seven patients, it was not possible to state that the dysfunction was or was not drug induced.

Usual Adult Dosage: Two tablets q.i.d.

Supplied: Light green tablets, imprinted "McNEIL" and "PARAFON FORTE"—bottles of 100 and 500.

0972

Caution: Federal law prohibits dispensing without prescription. Full directions for use should be read before administering or prescribing.

For information on symptoms/treatment of overdosage, see full prescribing information.

PARAFON FORTE tablets are manufactured by McNeil Laboratories Co., Dorado, PR 00646.

References: 1. Wallenstein SL, Houde RW: *Fed Proc* 13:414, 1954. 2. Batterman RC, Grossman AJ: *Fed Proc* 14:316, 1955. 3. Vickers FN: *Gastrointest Endosc* 14:94, 1967. 4. Fein FT: *Ann Allergy* 29:598, 1971. 5. Mielke CH, et al: *JAMA* 235:613, 1976. 6. Vernon WG: *Curr Ther Res* 14:801, 1972. 7. Miller AR: *Curr Ther Res* 19:444, 1976. 8. Walker JM: *Curr Ther Res* 15:249, 1973.

McNEIL

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Tail of whipworm
(*Trichuris trichiura*)

Vermox[®]: the only anthelmintic highly effective against whipworm.

	Cure Rate	Egg Reduction
VERMOX [®]	68%*	93%**
Mintezol ¹	35%†	45%††
Antiminth ²	Not Indicated	
Povan ³	Not Indicated	

Also highly effective against roundworm and hookworm

Since whipworm, roundworm and hookworm are all soil-borne helminths, mixed infections are not uncommon. Only one anthelmintic exhibits high efficacy rates for all three nematodes: whipworm—68%; roundworm—98%; hookworm—96%. That agent is VERMOX[®].

Please see following page for Summary of Prescribing Information.

Broad-spectrum coverage in mixed helminthic infections

Vermox[®] TABLETS
(mebendazole)



JANSSEN PHARMACEUTICA INC.
New Brunswick, N.J. 08903

Committed to research...
because so much remains to be done.

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JPI-023



**Broad-spectrum
coverage in mixed
helminthic infections**

TABLETS
Vermox[®]
(mebendazole)

Contraindications VERMOX is contraindicated in pregnant women (see: Pregnancy Precautions) and in persons who have shown hypersensitivity to the drug.

Precautions **PREGNANCY:** VERMOX has shown embryotoxic and teratogenic activity in pregnant rats at single oral doses as low as 10 mg/kg. Since VERMOX may have a risk of producing fetal damage if administered during pregnancy, it is contraindicated in pregnant women.

PEDIATRIC USE: The drug has not been extensively studied in children under two years; therefore, in the treatment of children under two years the relative benefit/risk should be considered.

Adverse Reactions Transient symptoms of abdominal pain and diarrhea have occurred in cases of massive infection and expulsion of worms.

Dosage and Administration The same dosage schedule applies to children and adults. The tablet may be chewed, swallowed or crushed and mixed with food. For the control of pinworm (enterobiasis), a single tablet is administered orally, one time.

For the control of roundworm (ascariasis), whipworm (trichuriasis), and hookworm infection, one tablet of VERMOX is administered, orally, morning and evening, on three consecutive days.

If the patient is not cured three weeks after treatment, a second course of treatment is advised. No special procedures, such as fasting or purging, are required.

* Mean cure rate of VERMOX[®] in treating whipworm; cure rate range of 61-75%. Data on file at Janssen Pharmaceutica Inc.

** Mean egg reduction of VERMOX[®] in treating whipworm; egg reduction range of 70-99%. Data on file at Janssen Pharmaceutica Inc.

† Rollo, I.M.: Drugs used in the chemotherapy of helminthiasis, in Goodman, L.S.; and Gilman, A. (eds.): *The Pharmacological Basis of Therapeutics*, ed. 5. New York, Macmillan, 1975, p. 1034.

†† Miller, M.J.; Krupp, I.M.; Little, M.D.; Santos, C.: Mebendazole an effective anthelmintic for trichuriasis and enterobiasis. *JAMA* 230 (10): 1412-1414, Dec. 9, 1974.

1. Registered trademark of Merck Sharp and Dohme.
2. Registered trademark of Roerig.
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*Committed to research...
because so much remains to be done.*

Health and Safety Tip

From the American Medical Association

535 North Dearborn Street/Chicago, Illinois 60610

Sun Tanning Harmful To Skin, Says AMA

Sun Tanning Harms Skin

What does your doctor think of sun tanning?

He's against it.

If you should ask your doctor whether there is any health value to sun tanning, he would have to answer "No." If you asked him whether sun tanning might hurt you, he would have to reply "Yes."

Sunning, overdone, can cause severe burn. Sunning, done modestly, can produce a golden tan that gives an illusion of health and well being. But that golden tan often leads to premature aging and wrinkling of the skin, to premature "age spots" on the hands and neck, and to skin cancer.

So, once again, the American Medical Association advises Americans everywhere against suntanning.

But, your doctor also is well aware that millions of Americans will ignore this advice this summer. They will flock to the swimming pools and beaches through the warm months to bask in the sun. They will stretch out on the grass in the back yard, or on the roof terrace, or in the nearest park.

If you insist on getting a tan this summer despite medical advice to the contrary,

here's how to do it without burning.

On the first day of sunning, allow 15 minutes on each side. The second day 20 minutes. The third day 25 to 30 minutes. By the third day the skin should begin to brown. Thereafter proceed at the best pace for your own skin to tan without burning. At the first sign of redness, get out of the sun.

It isn't easy to confine sun time to only half an hour on the first day at the vacation resort. But you can't stretch it very much. If you try to double the exposure time to hurry the tan, you'll burn. And then return from vacation with a peeling skin instead of a tan.

Time of exposure also should be adjusted to time of day. The sun's rays are hottest between 10 a.m. and 2 p.m. After 5 p.m. you aren't likely to burn much.

There are creams and lotions that screen some of the rays and reduce danger of burning. But if the cream should screen all rays, there would be no tanning. You can still burn through creams if you stay out long enough. Also, water in the pool or perspiration washes away much of the cream in a short time.

Tanning removes most of the natural oils from the surface of the skin and many sunbathers find it helpful to use a cream or oil to relieve dryness.

Enjoy the outdoor life of the summer months. Don't overdo the suntanning.



June, 1980
Frank Chappell
Science News Editor
AMA

NOTICIAS

AMA NEWS

STRESS FRACTURES PLAGUE JOGGERS

CHICAGO — Joggers are turning up in the doctor's office frequently these days. Often the joggers are suffering from painful stress fractures.

Thus doctors are studying better ways and means of finding these cracks early so that treatment can be started before the fracture becomes much more severe.

Joseph F. Nortray, MD, of the Department of Radiology, Henrotin Hospital, Chicago, reports in the April 25 Journal of the American Medical Association on a study of five runners who were patients at the Sports Clinic of the Illinois College of Podiatric Medicine last summer.

Dr. Nortray and colleagues tested a technique for diagnosing stress fractures early through use of radionuclide bone scans, supplementing conventional X-rays. They found that the radionuclide bone scan often would reveal the stress fracture earlier than conventional X-rays.

With the increase in jogging, there has been an associated increase of joggers seeking relief from pain in the feet and legs. The pain can be caused by arthritis, by muscle or tendon strains or by stress fractures, he says.

The symptom of the stress fracture is pain, pain that is relieved by rest. Conventional X-rays can delay an exact diagnosis from three weeks to three months after the pain begins.

The importance of early detection of stress fractures is early treatment, Dr. Nortray says. Undiagnosed stress fractures can progress to complete fractures.

"The best treatment for all stress fractures is rest from any activity that causes pain."

In other words, forget the old advice of the coach or trainer to "Run it off" when a sharp pain appears in the foot or leg. It might be a stress fracture.

POSTMARKETING STUDIES CONFIRM EFFECTIVENESS OF NEW ULCER DRUG

CHICAGO —Further postmarketing studies of a new drug for treating stomach ulcers have confirmed that the product is safe and effective.

The drug is cimetidine (Tagamet). It is one of a new class of products that in recent years have been so effective in treating stomach ulcers that it seldom is necessary today to operate on an ulcer patient.

In a report in the April 18 Journal of the American Medical Association, Lawrence M. Gifford, MD, and colleagues describe a study of the impact of cimetidine that was initiated seven months after its approval for marketing. Data were obtained from almost ten thousand patients over a three-month period.

Overall incidence of adverse effects reported was 4.4 per cent, and were virtually identical to side effects noted in premarketing testing, Dr. Gifford says. Adverse effects were nausea, vomiting, diarrhea, pain, cramps, dizziness and headache, in four or five of each hundred users.

More than 1,000 physicians throughout the nation cooperated with researchers at Smith Kline & French Laboratories, Philadelphia. Each doctor reported on an average of nine or ten patients who were receiving cimetidine.

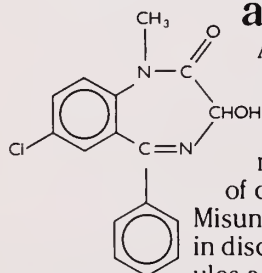
A promising new prescription drug is thoroughly tested for safety and effectiveness prior to marketing. The manufacturer is as certain as can be from tests in the laboratory, in animals, and finally, in humans that the product works and is safe.

But it sometimes happens that later, after the drug has been given to thousands of individuals, untoward results appear that were not revealed in the pre-marketing trials. The medical research community has long puzzled over how to conduct postmarket surveillance of a drug that is being prescribed by a hundred thousand doctors to several million patients.

Aspects of Management

What to tell your patients when you prescribe Valium® (diazepam/Roche)

Survey shows significant correlation between comprehension and compliance



A study of compliance patterns reveals that more than 6 out of 10 patients made errors in self-administration of prescribed medication, largely due to lack of comprehension.*

Misunderstanding of directions resulted in discrepancies in dosage schedules as well as in length of therapy.

Since evidence suggests that expanded verbal instructions may encourage compliance, the patient receiving Valium can benefit from your explanation of the dosage regimen, what response to expect from therapy and when to expect it.

What Valium (diazepam/Roche) can do

Your patients should know that 1) you are prescribing Valium as an adjunct to an overall program for the treatment of anxiety, and 2) Valium is given to relieve the symptoms of excessive anxiety and psychic tension while you help the patient to explore and deal with the underlying cause of his psychic tension.

Patients often interpret manifestations of anxiety, such as palpitations, hyperventilation, fatigue and muscle tension, as symptoms of a serious disease. However, when they



learn that these symptoms can be relieved by Valium therapy, patients can more readily understand the psychosomatic origin of their symptoms and to accept the nonpharmacologic measures you may recommend.

The time you devote to these explanations can be a therapeutic measure in itself. Most anxious patients respond to and benefit from a frank discussion with an objective, sympathetic professional.

At the start of treatment, establishing therapeutic goals helps the patient to learn *what* to expect and *when* to expect it. Patients should also be informed that the medication will be gradually reduced and discontinued upon attainment of the therapeutic goal.

Tapering of dosage is rarely necessary in short-term therapy, but when consistently higher doses are used for extended periods, patients should know that the gradual reduction of medication will be implemented in order to avoid sudden recurrence of symptoms or possible withdrawal symptoms.

Such recurrence is unlikely when the causes of the anxiety have been worked out satisfactorily within your overall treatment program.

What Valium (diazepam/Roche) can't do

It should be emphasized that there is no "magic" in any antianxiety tablet; that medication is not prescribed as a problem solver. Instead, Valium is being prescribed *as a temporary measure to relieve symptoms* generated by excessive anxiety and psychic tension.

* Boyd JR, et al: *Am J Hosp Pharm* 31: 485-491, May 1974

Before prescribing, please consult complete product information, a summary of which follows:

Indications: Tension and anxiety associated with anxiety disorders, transient situational disturbances and functional or organic disorders, psychoneurotic states manifested by tension, anxiety, apprehension, fatigue, depressive symptoms, or agitation, symptomatic relief of acute agitation, tremor, delirium tremens and hallucinosis due to acute alcohol withdrawal, adjunctively in skeletal muscle spasm due to reflex spasm to local pathology, spasticity caused by upper motor neuron disorders, athetosis, stiff-man syndrome, convulsive disorders (not for sole therapy). The effectiveness of Valium (diazepam/Roche) in long-term use, that is, more than 4 months, has not been assessed by systematic clinical studies. The physician should periodically reassess the usefulness of the drug for the individual patient.

Contraindicated: Known hypersensitivity to the drug. Children under 6 months of age. Acute narrow angle glaucoma, may be used in patients with open angle glaucoma who are receiving appropriate therapy.

Warnings: Not of value in psychotic patients. Caution against hazardous occupations requiring complete mental alertness. When used adjunctively in convulsive disorders,

possibility of increase in frequency and/or severity of grand mal seizures may require increased dosage of standard anticonvulsant medication, abrupt withdrawal may be associated with temporary increase in frequency and/or severity of seizures. Advise against simultaneous ingestion of alcohol and other CNS depressants. Withdrawal symptoms similar to those with barbiturates and alcohol have been observed with abrupt discontinuation, usually limited to extended use and excessive doses. Infrequently, milder withdrawal symptoms have been reported following abrupt discontinuation of benzodiazepines after continuous use, generally at higher therapeutic levels, for at least several months. After extended therapy, gradually taper dosage. Keep addiction-prone individuals under careful surveillance because of their predisposition to habituation and dependence.

Usage in Pregnancy: Use of minor tranquilizers during first trimester should almost always be avoided because of increased risk of congenital malformations as suggested in several studies. Consider possibility of pregnancy when instituting therapy; advise patients to discuss therapy if they intend to or do become pregnant.

Precautions: If combined with other psychotropics or anticonvulsants, consider carefully pharmacology of agents employed, drugs such as phenothiazines, narcotics,

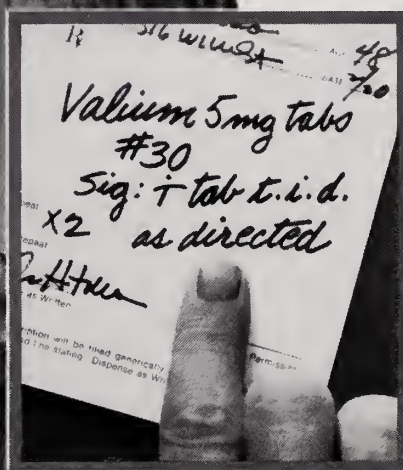
Practical pointers on taking antianxiety medications

do's Patients should be instructed to keep to their dosage schedule exactly as prescribed. If they miss a dose, they should not try to make it up by taking two doses the next time. Ask them to contact you promptly if they experience worrisome side effects.

Explain that drowsiness is a common reaction to almost all calming agents, but that it usually subsides in a few days. Urge the patient to contact you for a possible dosage adjustment if drowsiness or other reactions persist.

Just as you request a complete list of all medications the patient is taking, suggest that this list be given to any other physician treating her/him.

Like all medicines, Valium should be kept out of reach of children and young people. Old or unused medication should be discarded.



and don'ts Since drowsiness is an occasional problem, patients should be advised against driving or operating hazardous machinery until they see how the medication affects them. They should also know that tranquilizers increase the effects of alcoholic beverages, which should therefore be avoided. Also, warn patients against simultaneous use of drugs that depress the central nervous system, particularly sedative hypnotics.

Patients should be aware of the importance of not sharing their medications with friends and neighbors; they should know that what you have prescribed for them may be contraindicated for others.

2-mg, 5-mg, 10-mg scored tablets

Valium[®]

diazepam/Roche

An important adjunct to your treatment program for excessive psychic tension

Dosage: Individualize for maximum beneficial effect. *Adults:* Tension, anxiety and psychoneurotic states, 2 to 10 mg b.i.d. to q.i.d.; alcoholism, 10 mg t.i.d. or q.i.d. in first 24 hours, then 5 mg t.i.d. or q.i.d. as needed, adjunctively in skeletal muscle spasm, 2 to 10 mg t.i.d. or q.i.d., adjunctively in convulsive disorders, 2 to 10 mg b.i.d. to q.i.d. *Geriatric or debilitated patients:* 2 to 2½ mg, 1 or 2 times daily initially, increasing as needed and tolerated. (See Precautions.) *Children:* 1 to 2½ mg t.i.d. or q.i.d. initially, increasing as needed and tolerated (not for use under 6 months).

Supplied: Valium[®] (diazepam/Roche) Tablets, 2 mg, 5 mg and 10 mg—bottles of 100 and 500, Tel-E-Dose[®] packages of 100, available in trays of 4 reverse-numbered boxes of 25, and in boxes containing 10 strips of 10. Prescription Paks of 50, available in trays of 10.



Roche Laboratories
Division of Hoffmann-La Roche Inc.
Nutley, New Jersey 07110

barbiturates, MAO inhibitors and other antidepressants may potentiate its action. Usual precautions indicated in patients severely depressed, or with latent depression, or with suicidal tendencies. Observe usual precautions in impaired renal or hepatic function. Limit dosage to smallest effective amount in elderly and debilitated to preclude ataxia or oversedation.

Side Effects: Drowsiness, confusion, diplopia, hypotension, changes in libido, nausea, fatigue, depression, dysarthria, jaundice, skin rash, ataxia, constipation, headache, incontinence, changes in salivation, slurred speech, tremor, vertigo, urinary retention, blurred vision. Paradoxical reactions such as acute hyperexcited states, anxiety, hallucinations, increased muscle spasticity, insomnia, rage, sleep disturbances, stimulation have been reported; should these occur, discontinue drug. Isolated reports of neutropenia, jaundice, periodic blood counts and liver function tests advisable during long-term therapy.

STINGING ORGANISMS IN OCEANS ARE PLAGUE TO SWIMMERS

CHICAGO — Enjoy that trip to the seashore this summer, but keep in mind that there are many unpleasant little organisms in the ocean — things that sting like hot needles.

Some of them are so small and so transparent that you cannot see them. But you will soon know they are there when painful wheals appear on the skin.

Findlay E. Russell, MD, of the University of Southern California School of Medicine, Los Angeles, points out in a communication in the April 18 Journal of the American Medical Association that approximately 60 species of cnidarians (jellyfishes, hydroids, sea anemones, and corals) can sting vigorously.

The stinging marine organisms are common in the warmer waters of the Gulf of Mexico, the Pacific coast of Mexico and Atlantic coast of Florida.

It is not unusual that the organisms is not seen, Dr. Russell says. After storms or rough water, tentacles of many cnidarians break free and drift as small transparent pieces that still can sting. In particular, this is true of the Portuguese man-of-war, he says.

Some of the jellyfish are so tiny, less than two-tenths of an inch, that the swimmer becomes aware of their presence only when a sharp pain hits.

Immediate pain is severe and continues for several hours. The burning streaks and wheals subside after a few hours and the pain usually is gone by the next day.

There is no cure for the stings, other than medications to relieve the pain while healing occurs. Sometimes an inquiry of other swimmers or a life guard will determine whether anyone has been stung recently. If so, wisdom indicates that swimming should be ruled out for a day or two.

RESPIRATORY DISTRESS IN THE NEWBORN
MUST BE EVALUATED QUICKLY: SHOULD BE

ANTICIPATED

CHICAGO — Respiratory distress in newborn infants must be evaluated quickly and appropriate therapy planned, including transfer to a neonatal intensive care unit, an article appearing in the Journal of the American Medical Association urges.

That problem in the newborn can occur after any delivery but should be anticipated in high-risk infants, write Lisa K. Miller, MD, Leonid Calenoff, MD, and Melissa J. Riedy, MD, of the radiology department of Northwestern University Medical School, and John J. Boehm, MD, of the department of pediatrics of the same school.

High risk infants include those who are born prematurely, after a difficult labor, by caesarean section, or by diabetic mothers.

A chest roentgenogram is essential to differentiate among the many causes of respiratory distress, which encompass medically and surgically treatable conditions, the authors suggest.

An increased incidence of wet lung disease is noted. In the absence of congenital heart disease, which has an increased incidence in infants, the chest roentgenogram will return to normal a few weeks after birth.

Clinically, newborns with wet lung disease, a common cause of respiratory distress, develop tachypnea (excessive rapidity of respiration) shortly after birth. The condition clears up within two to five days.

Meconium aspiration syndrome and respiratory distress can be anticipated in the newborn with meconium-stained amniotic fluid. The particles from the aspirated meconium can cause bronchial obstruction with atelectasis (incomplete expansion of the lungs) and compensatory emphysema. Compensatory emphysema can lead to spontaneous pneumothorax, or subcutaneous emphysema. This can lead to superimposed bacterial pneumonia as a complication, the authors explain.

Unlike the relatively benign wet lung disease, the article asserts, hyaline membrane disease, known also as respiratory distress syndrome (RDS) carries a significant mortality. The use of assisted ventilation in the setting of newborn intensive care units, however, has cut down the death rate.

Infants of diabetic mothers are frequently

large for gestational age and often have cardiomegaly (a morbid condition characterized by enlargement of the heart with localized deposits of glycogen in the heart muscle) and hepatosplenomegaly (enlargement of the liver and the spleen).

Some causes of neonatal respiratory distress can be treated surgically but prompt recognition and treatment are essential.

NEW MEDICATIONS CURTAIL NEED FOR SURGERY ULCER TREATMENT

CHICAGO — What's new in ulcers?

Much, from the viewpoint of the sufferer. Most ulcers can now be treated with medications and there seldom is need for surgery today.

We are living in a new ulcer treatment era, says a survey report in the current issue of an American Medical Association specialty journal, *Archives of Surgery*.

New medications have made it possible to treat most ulcers with drugs, and it seldom is necessary to resort to surgery to cope with the painful internal ailment, says Israel Penn, MD, of Denver.

A recent research study planned in 14 Veterans Administration Hospitals to determine the effectiveness of a certain surgical treatment of duodenal ulcers had to be cancelled, Dr. Penn says. There weren't enough surgery patients to make a valid study.

Surgeons are enlisted today only for individuals with severe complications that fail to respond to drug treatment.

Along with new treatment methods that make surgery unnecessary there has been a marked decline in the total number of ulcers among Americans and Britons. There is only speculation as to the cause of this decline.

A number of new drugs are credited with the control of ulcers, particularly cimetidine, or Tagamet, says Dr. Penn. Many patients prefer taking three or four cimetidine tablets a day to the alternative (and

equally effective) treatment of intensive antacid administration, he says. The antacids must be taken in large amounts and sometimes cause diarrhea. Cimetidine produces a healing rate of from 69 to 100 per cent after four to six weeks of treatment.

It still is not known how long the ulcers will stay healed. Preliminary studies indicate a relapse rate of 15 to 20 percent. But many patients prefer to take several pills a day for the rest of their lives rather than have another operation, Dr. Penn reports.

Many other new drugs are now being tested that also may be useful in treating ulcers.

"Whether or not one or another of these new remedies will have a significant long-term impact on the management of these disorders remains to be seen."

NEWS RELEASE FROM THE PHARMACEUTICAL MANUFACTURERS CORPORATION

NEW TREATMENTS FOR LEUKEMIA AND HYPERTENSION, DEVICE TO STIMULATE BONE REGROWTH AND TEST TO DIAGNOSE HEART ATTACKS AMONG YEAR END APPROVALS

WASHINGTON, DC, March 13, 1980 — The U. S. Food and Drug Administration approved 14 new chemical entity prescription drugs in 1979, 13 of them products of member firms of the Pharmaceutical Manufacturers Association. Among the latest '79 approvals were a treatment for non-lymphocytic leukemia in adults, a drug to control severe hypertension and a treatment for a rare but life-threatening condition.

Medical device approvals late last year included a product that uses electrical current to promote healing of broken bones and a new test for the early diagnosis of heart attacks. Below is a description of each.

'Cerubidine' (daunorubicin hydrochloride) --

A new injectable drug to treat acute non-lymphocytic leukemia was researched and developed by Ives Laboratories, Inc.. (New York, NY) and approved for marketing by the FDA in December. Used as a single agent, Cerubidine has produced complete remission rates of 40 to 50 percent and in combination with cytarabine (another cancer remission drug) has led to complete remission rates of 53 to 65 percent. The drug should not be started in patients with pre-existing drug-induced bone marrow suppression unless the benefit from such treatment warrants the risk.

'Loniten' (minoxidil) -- Available for the treat-

ment of severe hypertension that is difficult to control. Loniten was researched and developed by The Upjohn Company (Kalamazoo, MI) and approved by the FDA in October. It relaxes and enlarges the arterioles, the body's smallest blood vessels, so that blood flows through them more easily. Most people with high blood pressure do not need the drug. Because of the potential for serious adverse effects, it should be taken only when a doctor decides that the patient's blood pressure is severe and other medicines are not working as intended.

'Demser' (metyrosine) -- A new drug to treat a rare but life-threatening condition called pheochromocytoma was approved by the FDA in October. While fewer than 1,000 Americans are afflicted each year with

this ailment, Merck Sharp & Dohme (Div. of Merck & Co., Inc., West Point, PA) developed 'Demser' in response to requests from medical specialists. The drug is designed to control drastic blood pressure increases caused by a rare tumor of the adrenal gland. It is not intended for the treatment of the common kind of high blood pressure.

'Direct Current Bone Growth Stimulator' -- A

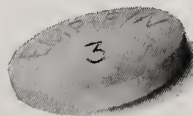
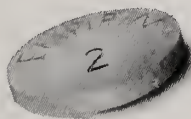
device that uses electrical current to promote healing of bone following fracture nonunion (bone broken completely apart) caused by trauma has been developed by Zimmer USA Inc., Warsaw, IN (subsidiary of Bristol Myers Co., NY NY). Approved by FDA in November, it appears to be particularly useful in treating nonunions which are resistant to other conventional methods. Thus, bone grafting and repeated surgery, often required for such fractures, can be avoided.

'ISOMUNE-LD' -- A low cost test for the early

diagnosis of heart attacks has been developed by Roche Diagnostics, division of Hoffmann-La Roche, Inc., Nutley, NJ. Approved by the FDA in October, it identifies the presence of LDH-1 isoenzyme, a substance liberated by dying heart muscle cells into the adjacent small veins. The test can be performed in any hospital laboratory at a cost of approximately one dollar for reagents -- substantially lower than the cost of an electrophoresis test for similar diagnoses.

~~EMPIRIN[®]~~ ~~COMPOUND~~ ~~CODEINE~~ IS NOW **EMPIRIN[®]** **CODEINE**

Each tablet contains: aspirin, 325 mg; plus codeine phosphate in one of the following strengths: # 2—15 mg (gr 1/4); # 3—30 mg (gr 1/2); # 4—60 mg (gr 1). (Warning—may be habit-forming)



**NO LONGER CONTAINS
PHENACETIN OR CAFFEINE.**



Burroughs Wellcome Co.
Research Triangle Park
North Carolina 27709

In recurrent urinary tract infections



Septra[®] DS

The background of the advertisement features a silhouette of a human torso. Overlaid on this is a white line drawing of the urinary tract, showing two kidneys at the top, connected by ureters to a central bladder at the bottom. The text is positioned within the central area of the torso, with the kidneys and bladder visible behind it.

Each tablet contains:
160 mg trimethoprim and 800 mg sulfamethoxazole

B.I.D.

**where
the action is.**

In the kidney

Septra DS provides effective anti-bacterial action in the kidneys, via urine and blood, against susceptible strains of E coli, Klebsiella-Enterobacter, Proteus mirabilis, Proteus vulgaris and Proteus morganii.

The high degree of efficacy of Septra DS was confirmed in a study of 59 patients with recurrent pyelonephritis. All patients had upper urinary tract disease as evidenced by fever $\geq 100.4^{\circ}$ F and/or flank pain, and $\geq 10^5$ organisms/ml of urine. After two weeks' therapy and up to seven days post-therapy, Septra achieved bacteriologic cure ($\leq 10,000$ organisms/ml of urine) in 91.5% of patients.¹

And during the critical "recurrence" period from one to four weeks post-therapy, this excellent response rate was well maintained. Of the 53 patients evaluated at that time, 51 (96.2%) were still infection free.¹

Unlike many other antibacterials for the treatment of urinary tract infections, Septra DS is administered on a convenient b.i.d. dosage schedule.

In the bladder

What makes Septra DS good for the tough areas—the kidneys—makes it good for the not-so-tough. Septra DS provides antibacterial action in the bladder, via urine and blood, against susceptible strains of major pathogens that cause recurrent cystitis.



And along the route to recurrence

During therapy, Septra DS diffuses into vaginal fluid² and into the bowel.^{3,4} By eliminating potential uropathogens from the fecal flora, and bathing the periurethral area in an "antibacterial" vaginal fluid, Septra DS helps block the most common route to reinfection in women.

Maintain adequate fluid intake and perform frequent urinalyses with careful microscopic examination during therapy. Septra is contraindicated in children under two months old.

Please see prescribing information on next page.



Burroughs Wellcome Co.
Research Triangle Park
North Carolina 27709

Septra® DS B.I.D.

Each tablet contains: 160 mg trimethoprim and 800 mg sulfamethoxazole

Septra® Suspension B.I.D.

Each teaspoonful (5 ml) contains: 40 mg trimethoprim and 200 mg sulfamethoxazole

Septra® DS Tablets Double Strength

Septra® Tablets

Septra® Suspension

INDICATIONS AND USAGE:

URINARY TRACT INFECTIONS: For the treatment of urinary tract infections due to susceptible strains of the following organisms: *Escherichia coli*, *Klebsiella-Enterobacter*, *Proteus mirabilis*, *Proteus vulgaris*, *Proteus morganii*. It is recommended that initial episodes of uncomplicated urinary tract infections be treated with a single effective antibacterial agent rather than the combination.

NOTE: Currently, the increasing frequency of resistant organisms is a limitation of the usefulness of all antibacterial agents, especially in the treatment of these urinary tract infections.

ACUTE OTITIS MEDIA: For the treatment of acute otitis media in children due to susceptible strains of *Haemophilus influenzae* or *Streptococcus pneumoniae* when in the judgment of the physician Septra offers some advantage over the use of other antimicrobial agents. Limited clinical information is presently available on the effectiveness of treatment of otitis media with Septra when the infection is due to *Haemophilus influenzae* resistant to ampicillin. To date, there are limited data on the safety of repeated use of Septra in children under two years of age. Septra is not indicated for prophylactic or prolonged administration in otitis media at any age.

SHIGELLOSIS: For the treatment of enteritis caused by susceptible strains of *Shigella flexneri* and *Shigella sonnei* when antibacterial therapy is indicated.

PNEUMOCYSTIS CARINII PNEUMONITIS: For the treatment of documented *Pneumocystis carinii* pneumonitis. To date, this drug has been tested only in patients 9 months to 16 years of age who were immunosuppressed by cancer therapy.

CONTRAINDICATIONS: Hypersensitivity to trimethoprim or sulfonamides. Pregnancy and during the nursing period. Infants less than two months of age.

WARNINGS: SEPTRA SHOULD NOT BE USED IN THE TREATMENT OF STREPTOCOCCAL PHARYNGITIS.

Clinical studies have documented that patients with Group A β -hemolytic streptococcal tonsillopharyngitis have a greater incidence of bacteriologic failure when treated with Septra than do those patients treated with penicillin as evidenced by failure to eradicate this organism from the tonsillopharyngeal area.

Deaths associated with administration of sulfonamides have been reported from hypersensitivity reactions, agranulocytosis, aplastic anemia and other blood dyscrasias. Experience with trimethoprim alone is much more limited, but occasional interference with hematopoiesis has been reported as well as an increased incidence of thrombopenia with purpura in elderly patients on certain diuretics, primarily thiazides.

Sore throat, fever, pallor, purpura or jaundice may be early signs of serious blood disorders. Frequent CBCs are recommended; therapy should be discontinued if a significant reduction in the count of any formed blood element is noted.

PRECAUTIONS: Use with caution in patients with impaired renal or hepatic function, possible folate deficiency, severe allergy or bronchial asthma. In glucose-6-phosphate dehydrogenase-deficient individuals, hemolysis may occur (frequently dose-related). During therapy, maintain adequate fluid intake and perform frequent urinalyses with careful microscopic examination and renal function tests, particularly where there is impaired renal function.

Since Septra may prolong prothrombin time in patients on warfarin, coagulation time should be reassessed when Septra is given.

ADVERSE REACTIONS: All major reactions to sulfonamides and trimethoprim are included, even if not reported with Septra. **Blood Dyscrasias:** Agranulocytosis, aplastic anemia, megaloblastic anemia, thrombopenia, leukopenia, hemolytic anemia, purpura, hypoprothrombinemia and methemoglobinemia. **Allergic Reactions:** Erythema multiforme, Stevens-Johnson syndrome, generalized skin eruptions, epidermal necrolysis, urticaria, serum sickness, pruritus, exfoliative dermatitis, anaphylactoid reactions, periorbital edema, conjunctival and scleral injection, photosensitization,

arthralgia and allergic myocarditis. **Gastrointestinal Reactions:** Glossitis, stomatitis, nausea, emesis, abdominal pains, hepatitis, diarrhea and pancreatitis. **C.N.S. Reactions:** Headache, peripheral neuritis, mental depression, convulsions, ataxia, hallucinations, tinnitus, vertigo, insomnia, apathy, fatigue, muscle weakness and nervousness. **Miscellaneous Reactions:** Drug fever, chills, and toxic nephrosis with oliguria and anuria. Periarthritis nodosa and L. E. phenomenon have occurred.

Due to certain chemical similarities to some goitrogens, diuretics (acetazolamide and the thiazides) and oral hypoglycemic agents, sulfonamides have caused rare instances of goiter production, diuresis and hypoglycemia; cross-sensitivity may exist with these agents. In rats, long-term administration of sulfonamides has produced thyroid malignancies.

DOSAGE AND ADMINISTRATION: Not recommended for use in infants less than two months of age.

URINARY TRACT INFECTIONS AND SHIGELLOSIS IN ADULTS AND CHILDREN AND ACUTE OTITIS MEDIA IN CHILDREN:

Adults: The usual adult dosage for the treatment of urinary tract infections is two tablets or four teaspoonfuls (20 ml) every 12 hours for 10 to 14 days. An identical daily dosage is used for 5 days in the treatment of shigellosis.

Children: The recommended dose for children with urinary tract infections or acute otitis media is 8 mg/kg trimethoprim and 40 mg/kg sulfamethoxazole per 24 hours, given in two divided doses every 12 hours for 10 days. An identical daily dosage is used for 5 days in the treatment of shigellosis. The following table is a guideline for the attainment of this dosage using Septra Tablets or Suspension.

Children: Two months of age or older:

Weight		Dose—every 12 hours	
lb	kg	Teaspoonfuls	Tablets
22	10	1 (5 ml)	1/2
44	20	2 (10 ml)	1
66	30	3 (15 ml)	1 1/2
88	40	4 (20 ml)	2 (or 1 DS tablet)

For patients with renal impairment:

Creatinine Clearance (ml/min)	Recommended Dosage Regimen
Above 30	Usual Standard Regimen
15-30	Half of the usual dosage regimen
Below 15	Use Not Recommended

PNEUMOCYSTIS CARINII PNEUMONITIS:

The recommended dosage for patients with documented *Pneumocystis carinii* pneumonitis is 20 mg/kg trimethoprim and 100 mg/kg sulfamethoxazole per 24 hours given in equally divided doses every 6 hours for 14 days. The following table is a guideline for the attainment of this dosage in children.

Weight		Dose—every 6 hours	
lb	kg	Teaspoonfuls	Tablets
18	8	1 (5 ml)	1/2
35	16	2 (10 ml)	1
53	24	3 (15 ml)	1 1/2
70	32	4 (20 ml)	2 (or 1 DS tablet)

HOW SUPPLIED: TABLETS, containing 80 mg trimethoprim and 400 mg sulfamethoxazole—bottles of 40, 100, 500 and 1000 tablets; unit dose pack of 100.

ORAL SUSPENSION, containing the equivalent of 40 mg trimethoprim and 200 mg sulfamethoxazole in each teaspoonful (5 ml), cherry flavored—bottle of 450 ml. Also available in double strength, oval-shaped, pink, scored tablets containing 160 mg trimethoprim and 800 mg sulfamethoxazole—Compliance™ Pak of 20, bottle of 60 and unit dose pack of 100.

REFERENCES:

(1) Data on file, Burroughs Wellcome Co. (2) Stamey TA, Condy M: The diffusion and concentration of trimethoprim in human vaginal fluid, in *Trimethoprim/Sulfamethoxazole: A Compilation of Clinical and Pharmacodynamic Studies in Chronic and Recurrent Urinary Tract Infections*. Science & Medicine Publishing Co, 1975, p 13. (3) Näff H: *Pathol Microbiol* 37:1, 1971. (4) Moorhouse EC, Farrell W: *J Med Microbiol* 6:249, 1973.



Burroughs Wellcome Co.
Research Triangle Park
North Carolina 27709

ROCHE

For recurrent attacks of urinary tract infection in women

BactrimTM DS Double Strength Tablets

Each tablet contains 160 mg trimethoprim and 800 mg sulfamethoxazole.

Just one tablet b.i.d. for 10 to 14 days



- Action at urinary/vaginal/lower bowel sites helps eliminate reservoirs of infecting organisms
- Distinctive antibacterial action plus wide spectrum helps eradicate recurrent UTI
- Low incidence of bacterial resistance in community practice

- Convenient *b.i.d.* dosage provides day-and-night antibacterial control
- Contraindicated during pregnancy and the nursing period. During therapy, maintain adequate fluid intake; perform CBC's and urinalyses with microscopic examination.

Before prescribing, please consult complete product information, a summary of which follows:

Indications and Usage: For the treatment of urinary tract infections due to susceptible strains of the following organisms: *Escherichia coli*, *Klebsiella-Enterobacter*, *Proteus mirabilis*, *Proteus vulgaris*, *Proteus morganii*. It is recommended that initial episodes of uncomplicated urinary tract infections be treated with a single effective antibacterial agent rather than the combination. *Note:* The increasing frequency of resistance limits the usefulness of all antibacterials, especially in these urinary tract infections.

Also for the treatment of documented *Pneumocystis carinii* pneumonia. To date, this drug has been tested only in patients 9 months to 16 years of age who were immunosuppressed by cancer therapy.

The recommended quantitative disc susceptibility method (Federal Register, 37:20527-20529, 1972) may be used to estimate bacterial susceptibility to Bactrim. A laboratory report of "Susceptible to trimethoprim-sulfamethoxazole" indicates an infection likely to respond to Bactrim therapy. If infection is confined to the urine, "Intermediate susceptibility" also indicates a likely response. "Resistant" indicates that response is unlikely.

Contraindications: Hypersensitivity to trimethoprim or sulfonamides; pregnancy; nursing mothers; infants less than two months of age.

Warnings: Deaths from hypersensitivity reactions, agranulocytosis, aplastic anemia and other blood dyscrasias have been associated with sulfonamides. Experience with trimethoprim is much more limited but occasional interference with hematopoiesis has been reported as well as an increased incidence of thrombocytopenia with purpura in elderly patients on certain diuretics, primarily thiazides. Sore throat, fever, pallor, purpura or jaundice may be early signs of serious blood disorders. Frequent CBC's are recommended; therapy should be discontinued if a significantly reduced count of any formed blood element is noted.

Precautions: Use cautiously in patients with impaired renal or hepatic function, possible folate deficiency, severe allergy or bronchial asthma. In patients with glucose-6-phosphate dehydrogenase deficiency, hemolysis, frequently dose-related, may occur. During therapy, maintain adequate fluid intake and perform frequent urinalyses, with careful microscopic examination, and renal function tests, particularly where there is impaired renal function.

Adverse Reactions: All major reactions to sulfonamides and trimethoprim are included, even if not reported with Bactrim. **Blood dyscrasias:** Agranulocytosis, aplastic anemia, megaloblastic anemia, thrombocytopenia, leukopenia, hemolytic anemia, purpura, hypoprothrombinemia and methemoglobinemia. **Allergic reactions:** Erythema multiforme, Stevens-Johnson syndrome, generalized skin eruptions, epidermal necrolysis, urticaria, serum sickness, pruritus, exfoliative dermatitis, anaphylactoid reactions, periorbital edema, conjunctival and scleral injection, photosensitization, arthralgia and allergic myocarditis. **Gastrointestinal reactions:** Glossitis, stomatitis, nausea, emesis, abdominal pains, hepatitis, diarrhea and pancreatitis. **CNS reactions:** Headache,

peripheral neuritis, mental depression, convulsions, ataxia, hallucinations, tinnitus, vertigo, insomnia, apathy, fatigue, muscle weakness and nervousness. **Miscellaneous reactions:** Drug fever, chills, toxic nephrosis with oliguria and anuria, periarteritis nodosa and L. E. phenomenon. Due to certain chemical similarities to some goitrogens, diuretics (acetazolamide, thiazides) and oral hypoglycemic agents, sulfonamides have caused rare instances of goiter production, diuresis and hypoglycemia in patients; cross-sensitivity with these agents may exist. In rats, long-term therapy with sulfonamides has produced thyroid malignancies.

Dosage: Not recommended for infants less than two months of age.

Urinary Tract Infections: Usual adult dosage—1 DS tablet (double strength), 2 tablets (single strength) or 4 teasp. (20 ml) b.i.d. for 10-14 days.

Recommended dosage for children—8 mg/kg trimethoprim and 40 mg/kg sulfamethoxazole per 24 hours, in two divided doses for 10 days. A guide follows:

Children two months of age or older

Weight		Dose—every 12 hours	
lbs	kgs	Teaspoonfuls	Tablets
20	9	1 teasp. (5 ml)	½ tablet
40	18	2 teasp. (10 ml)	1 tablet
60	27	3 teasp. (15 ml)	1½ tablets
80	36	4 teasp. (20 ml)	2 tablets or 1 DS tablet

For patients with renal impairment:

Creatinine Clearance (ml/min)	Recommended Dosage Regimen
Above 30	Usual standard regimen
15-30	½ the usual regimen
Below 15	Use not recommended

***Pneumocystis carinii* pneumonia:** Recommended dosage: 20 mg/kg trimethoprim and 100 mg/kg sulfamethoxazole per 24 hours in equal doses every 6 hours for 14 days. See complete product information for suggested children's dosage table.

Supplied: Double Strength (DS) tablets, each containing 160 mg trimethoprim and 800 mg sulfamethoxazole, bottles of 100, Tel-E-Dose[®] packages of 100 Tablets, each containing 80 mg trimethoprim and 400 mg sulfamethoxazole—bottles of 100 and 500; Tel-E-Dose[®] packages of 100; Prescription Paks of 40, available singly and in trays of 10. Oral suspension, containing in each teaspoonful (5 ml) the equivalent of 40 mg trimethoprim and 200 mg sulfamethoxazole, fruit-licorice flavored—bottles of 16 oz (1 pint).



Roche Laboratories
Division of Hoffmann-La Roche Inc.
Nutley, New Jersey 07110

Please see back cover.

Her next attack of cystitis may require

the Bactrim 3-system counterattack



ROCHE

Bactrim has shown high clinical effectiveness in recurrent cystitis as a result of its wide spectrum and distinctive antimicrobial action in the urinary, vaginal and lower intestinal tracts.

The probability of recurrent urinary tract infection appears to be enhanced by the establishment of large numbers of *E. coli* or other urinary pathogens on the vaginal introitus. The trimethoprim component of

Bactrim diffuses into vaginal fluid in effective concentrations, thus combating migration of pathogens into the urethra.

Studies have shown that Bactrim acts against *Enterobacteriaceae* in the bowel without the emergence of resistant organisms. Thus, Bactrim reduces the risk of intracolonic colonization by fecal uropathogens. It has no significant effect on other normal, necessary intestinal flora.

Bactrim fights uropathogens in the urinary tract/vaginal tract/lower intestinal tract

Please see reverse side for summary of product information.



BOLETIN

ASOCIACION MEDICA DE PUERTO RICO

CONTENIDO:

CARCINOMA OF THE STOMACH: EXPERIENCE AT THE UNIVERSITY HOSPITAL

OPERATION BY ALLIED HEALTH PERSONNEL OF A
LONG TERM HYPERTENSION DETECTION AND TREATMENT PROGRAM

ESOPHAGEAL ATRESIA AND TRACHEOESOPHAGEAL FISTULA-
A TEN YEAR REVIEW AT THE UNIVERSITY HOSPITAL

LEARNING PRIMARY CARE IN A PRIMARY CARE SETTING

ABDOMINAL HEART TRANSPLANTATION. THE SEARCH FOR AN
ALLOGRAFT EXTRATHORACIC PUMP. PRELIMINARY OBSERVATIONS

ABSTRACTOS DE LITERATURA MEDICA

MEDI-QUIZ (2)

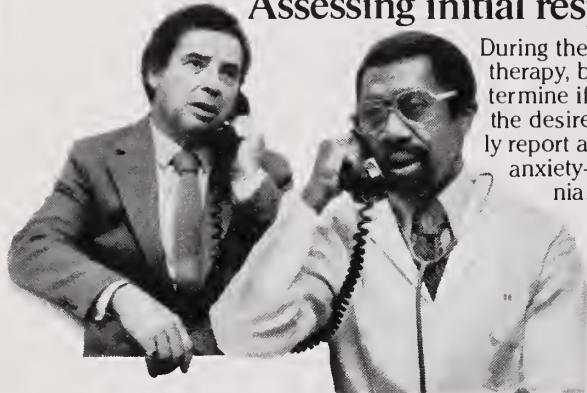
ELECTROCARDIOGRAM OF THE MONTH

CURSOS - NOTICIAS

INDICE PAGINA 290

Monitoring patient response to Valium® (diazepam/Roche)

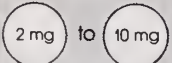

Assessing initial response to therapy



During the first follow-up visit after initiating therapy, both physician and patient should determine if Valium (diazepam/Roche) is having the desired effect. Most patients will promptly report a feeling of relaxation and relief of anxiety-linked symptoms such as insomnia, headaches, palpitations and hyperventilation. You will probably observe that the patient is calmer and more relaxed. If, however, patient response does not measure up to expectations, a reevaluation of the patient's profile with modification of the dosage regimen should be considered.



Making dosage adjustments

START	ADJUST
 2 mg to 10 mg 2x to 4x daily	

With any psychoactive medication it is good medical practice to initiate therapy at base dosage levels and titrate to the patient's needs. With Valium, experience has shown that 5 mg t.i.d. is usually sufficient although some patients with severe or persistent anxiety may require higher dosages initially. In geriatric or debilitated patients, the recommended dosage is 2 to 2½ mg once or twice daily.

When anxiety fluctuates, as is common with most patients, the dosage may be adjusted as needed during the course of therapy; three strengths in scored tablets give you unmatched flexibility and simplicity in individualizing dosage.

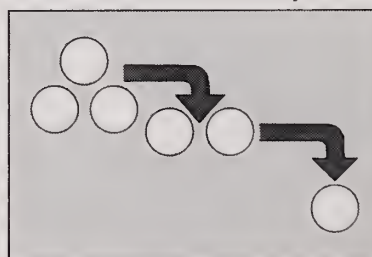
Evaluating progress toward therapeutic goals

SET GOALS						
		1	2	3	4	5
6	7	8	9	10	11	12
13	14	15	16	17	18	19
20	21	22	23	24	25	26
27	28	29	30	31		

At the beginning of therapy it is now common practice for both physician and patient to establish treatment goals and to estimate the amount of time needed to achieve them. Then the patient knows what to expect and when to expect it.

Some physicians find that compiling a checklist of present-ing symptoms and complaints is useful for assessing the patient's response from visit to visit. In this way, progress toward attainment of the therapeutic goal is reviewed at regular intervals. As patients feel their symptoms abate and begin to develop insight into the sources of their anxiety and psychic tension, the checklist can be expected to dwindle.

Discontinuing pharmacologic intervention



When you decide to discontinue therapy, tapering dosage is good medical practice. Although rarely necessary after short-term treatment with Valium, gradual dosage reduction is advisable for patients who have been on extended therapy. This gradual discontinuance should preclude either recurrence of pretreatment symptoms or development of untoward side effects. Symptoms of withdrawal have almost always been associated with abrupt discontinuance of therapy at higher dosages taken continuously over long periods of time.

2-mg, 5-mg, 10-mg scored tablets
Valium®
diazepam/Roche

An Important Adjunct to Your Treatment Program for Excessive Anxiety



See the following page for a summary of product information.

Valium® (diazepam/Roche) ®

Before prescribing, please consult complete product information, a summary of which follows:

Indications: Tension and anxiety associated with anxiety disorders, transient situational disturbances and functional or organic disorders; psychoneurotic states manifested by tension, anxiety, apprehension, fatigue, depressive symptoms or agitation; symptomatic relief of acute agitation, tremor, delirium tremens and hallucinosis due to acute alcohol withdrawal; adjunctively in skeletal muscle spasm due to reflex spasm to local pathology; spasticity caused by upper motor neuron disorders; atetosis, stiff-man syndrome, convulsive disorders (not for sole therapy).

The effectiveness of Valium (diazepam/Roche) in long-term use, that is, more than 4 months, has not been assessed by systematic clinical studies. The physician should periodically reassess the usefulness of the drug for the individual patient.

Contraindicated: Known hypersensitivity to the drug. Children under 6 months of age. Acute narrow angle glaucoma, may be used in patients with open angle glaucoma who are receiving appropriate therapy.

Warnings: Not of value in psychotic patients. Caution against hazardous occupations requiring complete mental alertness. When used adjunctively in convulsive disorders, possibility of increase in frequency and/or severity of grand mal seizures may require increased dosage of standard anticonvulsant medication; abrupt withdrawal may be associated with temporary increase in frequency and/or severity of seizures. Advise against simultaneous ingestion of alcohol and other CNS depressants. Withdrawal symptoms similar to those with barbiturates and alcohol have been observed with abrupt discontinuation, usually limited to extended use and excessive doses. Infrequently, milder withdrawal symptoms have been reported following abrupt discontinuation of benzodiazepines after continuous use, generally at higher therapeutic levels, for at least several months. After extended therapy, gradually taper dosage. Keep addiction-prone individuals under careful surveillance because of their predisposition to habituation and dependence.

Use in Pregnancy: Use of minor tranquilizers during first trimester should almost always be avoided because of increased risk of congenital malformations as suggested in several studies. Consider possibility of pregnancy when instituting therapy; advise patients to discuss therapy if they intend to or do become pregnant.

Precautions: If combined with other psychotropics or anticonvulsants, consider carefully pharmacology of agents employed, drugs such as phenothiazines, narcotics, barbiturates, MAO inhibitors and other antidepressants may potentiate its action. Usual precautions indicated in patients severely depressed, or with latent depression, or with suicidal tendencies. Observe usual precautions in impaired renal or hepatic function. Limit dosage to smallest effective amount in elderly and debilitated to preclude ataxia or oversedation.

Side Effects: Drowsiness, confusion, diplopia, hypotension, changes in libido, nausea, fatigue, depression, dysarthria, jaundice, skin rash, ataxia, constipation, headache, incontinence, changes in salivation, slurred speech, tremor, vertigo, urinary retention, blurred vision. Paradoxical reactions such as acute hyperexcited states, anxiety, hallucinations, increased muscle spasticity, insomnia, rage, sleep disturbances, stimulation have been reported, should these occur, discontinue drug. Isolated reports of neutropenia, jaundice, periodic blood counts and liver function tests advisable during long-term therapy.

Dosage: Individualize for maximum beneficial effect. **Adults:** Tension, anxiety and psychoneurotic states, 2 to 10 mg b.i.d. to q.i.d.; alcoholism, 10 mg t.i.d. or q.i.d. in first 24 hours, then 5 mg t.i.d. or q.i.d. as needed, adjunctively in skeletal muscle spasm, 2 to 10 mg t.i.d. or q.i.d., adjunctively in convulsive disorders, 2 to 10 mg b.i.d. to q.i.d. **Geriatric or debilitated patients:** 2 to 2½ mg, 1 or 2 times daily initially, increasing as needed and tolerated. (See Precautions.) **Children:** 1 to 2½ mg t.i.d. or q.i.d. initially, increasing as needed and tolerated (not for use under 6 months).

Supplied: Valium® Tablets, 2 mg, 5 mg and 10 mg—bottles of 100 and 500; Tel-E-Dose® packages of 100, available in trays of 4 reverse-numbered boxes of 25, and in boxes containing 10 strips of 10. Prescription Paks of 50, available in trays of 10.

Roche Laboratories
Division of Hoffmann-La Roche Inc.
Nutley, New Jersey 07110

LISTA DE ANUNCIANTES

BOEHRINGER INGELHEIM
Catapres

Mc NEIL LAB.
Haldol
Parafon Forte
Tylenol w Codeine

NORWICH INTERNATIONAL
Macrochantin

PFIZER CORPORATION
Diabinese

ROCHE LAB.
Librium
Valium

SMITH, KLINE & FRENCH
Tagamet

SMITH KLINE DIAGNOSTICS
Hemocult

SYNTEX LAB.
Neo-Mull-Soy

U. S. V. PHARM.
Hygroton

THE UPJOHN COMPANY
Motrin

WILLIAM H. RORER
Perdiem

THE FRANCIS & TAYLOR
LIBRARY OF MEDICINE
BOSTON
SEP 23 1980





Lung cancer is now an equal opportunity tragedy.

Remember when lung cancer was a man's disease. Because men had been smoking longer than women. But the women's smoking boom that started in the 1930's and 40's—is paying most cruel dividends today. Yet most people still think lung cancer is a man's disease. Tell your female patients the true story. That lung cancer is now an equal opportunity tragedy. That's what "you've come a long way, baby" is all about.

BOLETIN

ASOCIACION MEDICA DE PUERTO RICO

(USPS-060000)

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Fundado en 1903

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Trabajos Científicos:

El Boletín acepta para su publicación artículos relativos a medicina y cirugía y las ciencias afines. Igualmente acepta artículos especiales y correspondencia que pudiera ser de interés general para la profesión médica. El artículo, si se aceptara, será con la condición de que se publicará únicamente en esta revista. La AMPR no se hace responsable de las opiniones y declaraciones vertidas por los autores y sus puntos de vista no necesariamente representan aquellos de la AMPR, cualquier relación con la política oficial es coincidencia.

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ASOCIACION MEDICA DE PUERTO RICO

VOLUMEN 72

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Health and Safety Tip

From the American Medical Association

535 North Dearborn Street/Chicago, Illinois 60610

Intelligent Patient Gets Better Care

Patients Can Help

Being an intelligent patient may reduce your medical bills and help you obtain better health care.

Learning to work with your doctor is the beginning of the process, the American Medical Association points out.

First, choose a family physician. Make an appointment for an examination, so you can get to know him and he can get to know you. Then if you become ill or injured you will know whom to turn to.

There is a real advantage in going to the doctor's office, rather than attempting to get him to come to your home. It is to your advantage to be examined where all necessary equipment and allied health workers are present. It also saves money.

Before phoning for an

emergency appointment, collect your thoughts and be prepared to list symptoms. If you brief the doctor properly, he may be able to give advice by phone. Or he may counsel you to come to his office. If there is a real emergency, he may suggest that you meet at the hospital.

Make the most of the medical time you are paying for in the doctor's office. Have in mind important facts about past illnesses, operations, and accidents. Have your questions ready, and do not apologize for asking. Full information about your health is important to your well being. You go to the doctor for two things: his opinion and his advice. Be sure you are well satisfied on both counts.

Don't hesitate to ask about fees. Your doctor would prefer that you open the subject, since you are aware of your own financial situation, and he is not.

No one would dream of buying a pair of new shoes and throwing one of them away. Yet, some people leave their doctor's office with a prescription and some advice and do nothing about either. You've paid for the advice. Follow it.



March, 1980
Frank Chappell
Science News Editor
AMA

AVISO DE INTERES

La Junta Editora, consciente de su responsabilidad de hacer que el "Boletín" cumpla a cabalidad con su cometido de divulgar conocimientos médicos, elevar las normas de educación médica y al propio tiempo de llenar las necesidades de todos los compañeros médicos, ha acordado establecer una nueva Sección que se conocerá como "Sección de Preguntas".

Bajo esta nueva Sección, todos los compañeros tendrán la oportunidad de enviarnos preguntas médicas de casos difíciles o casos clínicos para opinión experta. Estas preguntas, con sus respuestas, serán publicadas en esta nueva Sección.

Las preguntas deberán ser enviadas a:

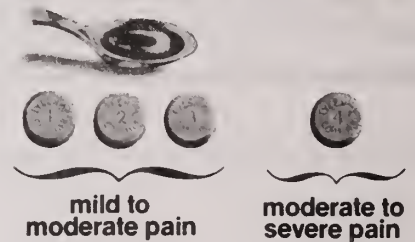
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Sección de Preguntas
Apartado 9387
Santurce, P. R. 00908

Esperamos sus preguntas.

Juan M. Aranda, MD
Presidente
Junta Editora

TYLENOL® with Codeine

tablets  / elixir 



Summary of Prescribing Information

Description

Tablets: Contain codeine phosphate* No. 1—7.5 mg. (1/4 gr.); No. 2—15 mg. (1/2 gr.); No. 3—30 mg. (1/2 gr.); No. 4—60 mg. (1 gr.)—plus acetaminophen 300 mg.

Elixir: Each 5 ml. contains 12 mg. codeine phosphate* plus 120 mg. acetaminophen (alcohol 7%).

*Warning: May be habit forming

Actions: Acetaminophen is an analgesic and antipyretic; codeine an analgesic and antitussive

Contraindications: Hypersensitivity to acetaminophen or codeine

Warnings: *Drug dependence:* Codeine can produce drug dependence of the morphine type and may be abused. Dependence and tolerance may develop upon repeated administration, prescribe and administer with same caution appropriate to other oral narcotics. Subject to the Federal Controlled Substances Act.

Usage in ambulatory patients: Caution patients that codeine may impair mental and/or physical abilities required for performance of potentially hazardous tasks such as driving a car or operating machinery.

Interaction with other CNS depressants: Patients receiving other narcotic analgesics, general anesthetics, phenothiazines, other tranquilizers, sedative-hypnotics or other CNS depressants (including alcohol) with this drug may exhibit additive CNS depression. When such a combination is contemplated, reduce the dose of one or both agents.

Usage in pregnancy: Safe use not established. Should not be used in pregnant women unless potential benefits outweigh possible hazards.

Pediatric use: Safe dosage of this combination has not been established in children below the age of three.

Precautions: *Head injury and increased intracranial pressure:* Respiratory depressant effects of narcotics and their capacity to elevate cerebrospinal fluid pressure may be markedly exaggerated in the presence of head injury, other intracranial lesions or a pre-existing increase in intracranial pressure. Narcotics produce adverse reactions which may obscure the clinical course of patients with head injuries.

Acute abdominal conditions: Codeine or other narcotics may obscure the diagnosis or clinical course of acute abdominal conditions.

Special risk patients: Administer with caution to certain patients such as the elderly or debilitated and those with severe impairment of hepatic or renal function, hypothyroidism, Addison's disease, and prostatic hypertrophy or urethral stricture.

Adverse Reactions: Most frequent: lightheadedness, dizziness, sedation, nausea and vomiting, more prominent in ambulatory than nonambulatory patients, some of these reactions may be alleviated if the patient lies down. Others: euphoria, dysphoria, constipation and pruritus.

Dosage and Administration: Dosage should be adjusted according to the severity of the pain and the response of the patient. It may occasionally be necessary to exceed the usual dosage recommended below in cases of more severe pain or in those patients who have become tolerant to the analgesic effect of narcotics. TYLENOL with Codeine tablets are given orally. The usual adult dose is: Tablets No. 1, No. 2, and No. 3. One or two tablets every four hours as required. Tablets No. 4. One tablet every four hours as required. TYLENOL with Codeine elixir is given orally. The usual doses are: **Children (3 to 6 years):** 1 teaspoonful (5 ml.) 3 or 4 times daily; **(7 to 12 years):** 2 teaspoonfuls (10 ml.) 3 or 4 times daily; **(under 3 years):** safe dosage has not been established. **Adults:** 1 tablespoonful (15 ml.) every 4 hours as needed.

Drug Interactions: CNS depressant effect may be additive with that of other CNS depressants. See Warnings.

For information on symptoms/treatment of overdosage, see full prescribing information.

Full directions for use should be read before administering or prescribing.

TYLENOL with Codeine tablets are manufactured by McNeil Laboratories Co., Dorado, Puerto Rico 00646.

Caution: Federal law prohibits dispensing without prescription.

© McNEILAB, Inc. 1980

08721

McNEIL

McNeil Laboratories, McNEILAB, Inc.
Fort Washington, PA 19034

Sprains and Strains

Potent pain relief without aspirin complications



TYLENOL[®] with Codeine

tablets  / elixir 

Tablets Contain acetaminophen 300 mg plus codeine phosphate* as follows:
No.1—7.5 mg (1/8 gr); No.2—15 mg (1/4 gr); No.3—30 mg (1/2 gr); No.4—60 mg (1 gr)
Elixir Each 5 ml contains 12 mg codeine phosphate* plus 120 mg acetaminophen (Alcohol 7%)

*Warning: May be habit forming.

A full-page photograph of a kayaker in a white helmet and orange life vest, paddling through white water rapids. The kayaker is wearing a green and yellow striped shirt. The water is splashing around the kayak, which is orange and yellow. The background is dark and rocky.

Control when it's needed

**When diet alone fails in maturity-onset diabetes...
the addition of Diabinese® (chlorpropamide) to diet
may make the difference.**

Diet and Diabinese helps reduce elevated blood glucose levels. Moreover, patients who have shown an inadequate response to diet and another oral antidiabetic agent may benefit from a switch to diet and Diabinese.

Diet and Diabinese is the most widely prescribed oral antidiabetic regimen.

**Diabinese helps provide full 24-hour control of
blood sugar with just one convenient dose a day.**

Patients are more likely to adhere to this simple treatment schedule, less likely to miss doses over the long term.

**When diet alone fails to effectively lower elevated
blood sugar levels in maturity-onset diabetes...**

Diet & Diabinese®

(chlorpropamide)

100-mg and 250-mg Tablets

Pfizer

LABORATORIES DIVISION
Pfizer Inc.

**Leaders in
Oral Diabetic Therapy**

See following page for Brief Summary of Diabinese prescribing information, including contraindications and adverse reactions.

When diet alone fails
in maturity-onset diabetes and
an oral agent is indicated...

DIABINESE® (chlorpropamide) Tablets

100 mg and 250 mg

BRIEF SUMMARY

DIABINESE® (chlorpropamide) Tablets

Contraindications: Diabinese is not indicated in patients having juvenile or growth-onset diabetes mellitus, severe or unstable "brittle" diabetes, and diabetes complicated by ketosis and acidosis, diabetic coma, major surgery, severe infection, or severe trauma.

Diabinese is contraindicated during pregnancy. Serious consideration should be given to the potential hazard of its use in women of childbearing age who may become pregnant.

Diabinese is contraindicated in patients with serious impairment of hepatic, renal, or thyroid function.

Precautions: Use chlorpropamide with caution with barbiturates, in patients with Addison's disease or in those ingesting: alcohol, antibacterial sulfonamides, phenylbutazone, salicylates, probenecid, dicoumarol or MAO inhibitors.

Warnings: DIABINESE (CHLORPROPAMIDE) SHOULD NOT BE USED IN JUVENILE DIABETES OR IN DIABETES COMPLICATED BY ACIDOSIS, COMA, SEVERE INFECTION, MAJOR SURGICAL PROCEDURES, SEVERE TRAUMA, SEVERE DIARRHEA, NAUSEA AND VOMITING, ETC.

HYPOGLYCEMIA, IF IT OCCURS, MAY BE PROLONGED.

Adverse Reactions: Usually dose-related and generally respond to reduction or withdrawal of therapy. Generally transient and not of a serious nature and include anorexia, nausea, vomiting and gastrointestinal intolerance; weakness and paresthesias.

Certain untoward reactions associated with idiosyncrasy or hypersensitivity have occasionally occurred, including jaundice (rarely associated with severe diarrhea and bleeding), skin eruptions rarely progressing to erythema multiforme and exfoliative dermatitis, and probably depression of formed elements of the blood. With a few exceptions, these manifestations have been mild and readily reversible on the withdrawal of the drug.

Diabinese should be discontinued promptly when the development of sensitivity is suspected.

Jaundice has been reported, and is usually promptly reversible on discontinuance of therapy. THE OCCURRENCE OF PROGRESSIVE ALKALINE PHOSPHATASE ELEVATION SHOULD SUGGEST THE POSSIBILITY OF INCIPIENT JAUNDICE AND CONSTITUTES AN INDICATION FOR WITHDRAWAL OF THE DRUG.

Leukopenia, thrombocytopenia and mild anemia, which occur occasionally, are generally benign and revert to normal, following cessation of the drug.

Cases of aplastic anemia and agranulocytosis, generally similar to blood dyscrasias associated with other sulfonylureas, have been reported.

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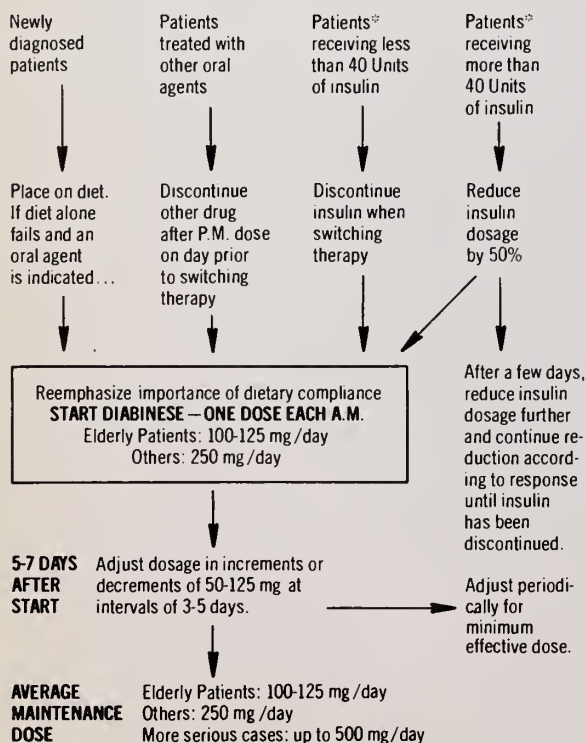
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After five to seven days following initiation of therapy, dosage may be adjusted upward or downward in increments of 50 to 125 mg at intervals of three to five days. Patients who do not respond completely to 500 mg daily will usually not respond to higher doses. Maintenance doses above 750 mg daily should be avoided.

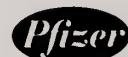
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CARCINOMA OF THE STOMACH: EXPERIENCE AT THE UNIVERSITY HOSPITAL

Manuel E. Lores, MD, Rafael Sorrentino, MD, FACS, Luis Vallecillo, MD,
FACS and Pedro J. Rossello, MD, FACS, FAAP

Summary: We reviewed the records of 394 patients with histologically proven carcinoma of the stomach from 1960 to 1972. Gastric cancer predominated in males, with ratio of men to women of 2.5 to 1. Eighty one percent of patients were from 50 to 80 years. The most frequent complaints on admission were abdominal pain (40 percent) and weight loss (25 percent), and the most common physical findings were weight loss (30 percent) and a palpable abdominal mass (25 percent). The operability rate was 84 percent and the resectability rate was 53 percent. Fifty one patients (13 percent) were found to have localized disease, 213 patients (54 percent) had regional metastasis and the remaining 130 pts (33 percent) had distant metastatic spread. The operative procedures performed in 334 patients included: subtotal gastrectomy (42 percent), total gastrectomy (13 percent), esophagogastrectomy (8 percent), gastrojejunostomy (17 percent), and exploration plus biopsy (20 percent). The overall operative mortality was 20 percent. The five-

year survival rate (8.4 percent overall) varied from 3.8 percent after esophagogastrectomy to 19 percent after subtotal gastrectomy, and to 35 percent for those with localized disease. Subtotal gastrectomy gave the best results in this series, whether measured in terms of median or five-year survival. Esophagogastrectomy and by-pass procedures had high operative mortality and low surgical rates, and should be reserved for special conditions.

Resumen: Durante el período de 13 años comprendido entre enero de 1960 y diciembre de 1972 aparecen registrados 394 pacientes con diagnóstico histológico de cáncer de estómago en el registro de neoplasia del Centro de Cáncer del Hospital Universitario. Los expedientes médicos de estos 394 pacientes fueron revisados y analizados para factores relacionados con la distribución por edad y sexo, tasa de operabilidad y resectabilidad, manifestaciones clínicas, estadio de la enfermedad, tipo de operaciones realizadas, mortalidad operatoria y sobrevivida a 5 años. Existe una mayor incidencia en el sexo masculino con una relación de 2.5 a 1. La edad del 81 por ciento de los pacientes estaba comprendida entre los 50 y 80 años. La tasa de operabilidad fue 84 por ciento y la de resección gástrica 53 por ciento. Dolor abdominal y pérdida de peso fueron los síntomas prin-

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TABLE I

Age and Sex Distribution - 394 Patients

Sex	A G E							Total
	< 20	20-30	30-40	40-50	50-60	60-70	70 +	
Male	0	3 (1 o/o)	11 (4 o/o)	32 (11 o/o)	63 (23 o/o)	98 (35 o/o)	73 (26 o/o)	280 (71 o/o)
Female	1 (1 o/o)	3 (2 o/o)	6 (5 o/o)	17 (15 o/o)	18 (16 o/o)	34 (30 o/o)	35 (31 o/o)	114 (29 o/o)
Total	1 (0.25 o/o)	6 (1.5 o/o)	17 (4.3 o/o)	49 (12.4 o/o)	81 (20.5 o/o)	132 (33.5 o/o)	108 (27.5 o/o)	394 (100 o/o)

cipales, mientras que en el examen físico los hallazgos más frecuentes fueron pérdida de peso y una masa abdominal palpable. En cuanto al estadio de la enfermedad, 33 por ciento de los pacientes tenían enfermedad generalizada, 54 por ciento enfermedad regional y el 13 por ciento restante enfermedad localizada. Gastrectomía subtotal fue la operación más frecuentemente empleada (42 por ciento), seguida por laparotomía exploratoria y biopsia (20 por ciento), gastroyeyunostomía (17 por ciento), gastrectomía total (13 por ciento) y esogagogastrectomía (8 por ciento). La mortalidad operatoria general fue 20 por ciento. La sobrevida a 5 años fue 35 por ciento en aquellos pacientes con enfermedad localizada y 8.4 por ciento en general. Los resultados obtenidos con las diferentes operaciones empleadas son discutidos y analizados.

National Cancer Survey showed a 63 percent decrease in the incidence of gastric cancer during the two decades from 1960 to 1970 (1). Although the incidence and total mortality of stomach carcinoma has declined since 1950, the prognosis remains poor. Cady has claimed that "no progress in the surgical management of this disease has been accomplished since 1950, despite a generally aggressive surgical approach" (2). In Europe and North America this statement seems to be true despite apparent advances in diagnostic and therapeutic techniques. We have, therefore, been motivated to review our own experience in dealing with gastric cancer in an effort to delineate features that may determine the outcome in our local environment at the University Hospital.

Patients and Methods

The National Cancer Institute's Third

The tumor registry at the University Hospi-

TABLE II
 Most Common Symptoms and Physical Findings

<i>Symptoms</i>	<i>No. of Patients</i>	<i>Percent</i>
<i>ABDOMINAL PAIN</i>	<i>157</i>	<i>40</i>
<i>WEIGHT LOSS</i>	<i>98</i>	<i>25</i>
<i>VOMITING</i>	<i>78</i>	<i>20</i>
<i>WEAKNESS</i>	<i>66</i>	<i>17</i>
<i>Physical Findings</i>	<i>No. of Patients</i>	<i>Percent</i>
<i>WEIGHT LOSS</i>	<i>118</i>	<i>30</i>
<i>ABDOMINAL MASS</i>	<i>98</i>	<i>25</i>
<i>CERVICAL NODES</i>	<i>39</i>	<i>10</i>
<i>RECTAL SHELF</i>	<i>12</i>	<i>3</i>

tal recorded 394 patients with histologically proven adenocarcinoma of the stomach from 1960 to 1972. Follow-up and final outcome data was available in all patients. Records of these 394 patients were reviewed and analyzed for factors related to age and sex distribution, operability rate and type of operation, clinical manifestations, stage of disease, operative mortality and five-year survival.

Results

Age and Sex Distribution (Table I)

There is a predominance of males, with 2.5 to 1 ratio over females (280:114). The most common age of presentation was the seventh decade of life (33 percent) and

81 percent of the patients were 50 years or older.

Clinical Manifestations (Table II)

The chief complaints on admission were abdominal pain (40 percent), weight loss (25 percent), and vomiting (20 percent). The most common physical findings were weight loss (30 percent), a palpable abdominal mass (25 percent) and palpable cervical nodes (10 percent).

Operability and Resectability Rates (Table III)

An abdominal operation ranging from exploration and biopsy to total gastrectomy

TABLE III
UDH 394 Gastric Cancer Cases (1960-1972)

	Number	Percent
NOT OPERATED	60	15.3
OPERATED	334	84
GASTRIC RESECTION	211	53

TABLE IV
Stage of Disease in 394 Cases of Gastric Cancer

Stage	Number	Percent
LOCALIZED	51	13
REGIONAL	213	54
DISTANT	130	33

was done in 334 patients (84 percent). The resectability rate for the 394 patients was 53 percent.

Stage of Disease (Table IV)

Only fifty one patients (13 percent) were found to have localized disease. Two hundred and thirteen patients (54 percent) had regional metastasis and 130 patients (33 percent) had distant metastasis.

Operative Therapy (Table V)

Among the 334 operations performed,

191 (57 percent) were palliative, 78 (23 percent) curative and 65 (19 percent) diagnostic.

Subtotal gastrectomy was the most common operation performed (142 patients, 42 percent), followed in frequency by exploration and biopsy (65 patients, 20 percent), gastrojejunostomy (58 patients, 17 percent), total gastrectomy (143 patients, 13 percent) and esophagogastrectomy (26 patients, 8 percent).

Operative Mortality (Table VI)

Operative mortality is defined as death within one month following the surgical pro-

TABLE V
Type of Operation in 334 Patients

<i>Procedure</i>	<i>Number</i>	<i>Percent</i>
<i>SUBTOTAL GASTRECTOMY</i>	<i>142</i>	<i>42</i>
<i>TOTAL GASTRECTOMY</i>	<i>43</i>	<i>13</i>
<i>ESOPHAGOGASTRECTOMY</i>	<i>26</i>	<i>8</i>
<i>GASTROJEJUNOSTOMY</i>	<i>58</i>	<i>17</i>
<i>EXPLORATORY LAPAROTOMY AND BIOPSY</i>	<i>65</i>	<i>20</i>
<i>TOTAL</i>	<i>334</i>	<i>100</i>

cedure. The operative mortality was 20 percent among the 334 patients operated. This ranged from a high of 34 percent after exploration and biopsy to a low of 11 percent for total gastrectomy. The operative mortality also varied with regards to whether the operation was a curative (5 percent), palliative (22 percent) or diagnostic (34 percent) procedure.

Five-Year Survival (Table VII)

The overall five-year survival was 8.4 percent and ranged from 3.8 percent after esophagogastrectomy to 19 percent after subtotal gastrectomy. The staging of the disease correlated significantly with survival for all three categories of involvement (localized - 35 percent, regional - 6.5 percent and distant - 0.8 percent).

Mean and Median Survival Time (Table VIII)

Average and median survival in months after the different operations performed are summarized in this table. There is no significant difference in the laparotomy and biopsy group as compared to the gastrojejunostomy group.

Discussion

The entire group of patients in this series had their cancer diagnosed prior to January 1, 1973 and were eligible for five-year survival analysis.

In the most recently reported series of stomach cancer the overall five-year survival varies between 8 percent and 11 percent and is approximately 30 percent in patients who have localized disease and curative procedures (3, 4, 5, 6, 7). Five-year survival in our series is 8.4 percent overall, 35 percent for those

TABLE VI

Operative Mortality

<i>Procedure</i>	<i>Number of Cases</i>	<i>Deaths</i>	<i>Operative Mortality - Percent</i>
<i>OVERALL</i>	<i>334</i>	<i>68</i>	<i>20 percent</i>
<i>PALLIATIVE</i>	<i>191</i>	<i>42</i>	<i>22 percent</i>
<i>CURATIVE</i>	<i>78</i>	<i>4</i>	<i>5 percent</i>
<i>DIAGNOSTIC</i>	<i>65</i>	<i>22</i>	<i>34 percent</i>
<i>ESOPHAGOGASTRECTOMY</i>	<i>26</i>	<i>5</i>	<i>19 percent</i>
<i>TOTAL GASTRECTOMY</i>	<i>43</i>	<i>5</i>	<i>11 percent</i>
<i>SUBTOTAL GASTRECTOMY</i>	<i>142</i>	<i>18</i>	<i>12 percent</i>
<i>GASTROJEJUNOSTOMY</i>	<i>58</i>	<i>18</i>	<i>31 percent</i>
<i>EXPLORATORY LAPAROTOMY AND BIOPSY</i>	<i>65</i>	<i>22</i>	<i>34 percent</i>

with localized disease and 30 percent for patients undergoing resection for cure.

Subtotal gastrectomy, the procedure performed most frequently, had the highest number of survivors, 27, with an overall five-year survival of 19 percent. Five of the 43 patients who had total gastrectomy survived five years, resulting in a discouragingly low survival rate of 11 percent. This is similar to data reported elsewhere (7).

Five percent of the 191 patients described by the surgeons as having palliative procedures became five-year survivors. This apparently contradictory finding has been previously reported in the literature (5) and serves to emphasize the importance of vigo-

rous attempts to eliminate tumor bulk during the original operative procedure, since this may not only aid in palliation but also may be on occasion associated with long-term survival. Esophagogastrectomy was done in 26 patients with only one patient surviving five years. The average survival after this procedure was shorter than after any ablative procedure. The operability and resectability rates in our series, 84 percent and 53 percent respectively, are similar to those in other series (3, 5, 7). The overall operative mortality rate was 20 percent. The 65 diagnostic procedures (exploration and biopsy) resulted in a 34 percent operative mortality, indicating the high risk for simple procedures

TABLE VII

Five-Year Survival

<i>Group</i>	<i>Number</i>	<i>Five - Year Survival Percent</i>
<i>ALL PATIENTS</i>	<i>394</i>	<i>8.4</i>
<i>MALES</i>	<i>280</i>	<i>9</i>
<i>FEMALES</i>	<i>114</i>	<i>7</i>
<i>LOCALIZED DISEASE</i>	<i>51</i>	<i>35</i>
<i>REGIONAL DISEASE</i>	<i>213</i>	<i>6.5</i>
<i>DISTANT DISEASE</i>	<i>130</i>	<i>0.8</i>
<i>ESOPHAGOGASTRECTOMY</i>	<i>26</i>	<i>3.8</i>
<i>SUBTOTAL GASTRECTOMY</i>	<i>142</i>	<i>19</i>
<i>TOTAL GASTRECTOMY</i>	<i>43</i>	<i>11.6</i>
<i>PALLIATIVE PROCEDURES</i>	<i>191</i>	<i>5.2</i>
<i>CURATIVE PROCEDURES</i>	<i>78</i>	<i>29.5</i>

TABLE VIII

Mean and Median Survival Time

<i>Operation</i>	<i>Mean Survival (Months)</i>	<i>Median Survival (Months)</i>
<i>EXPLORATORY LAPAROTOMY AND BIOPSY</i>	<i>3</i>	<i>3</i>
<i>GASTROJEJUNOSTOMY</i>	<i>5</i>	<i>4</i>
<i>ESOPHAGOGASTRECTOMY</i>	<i>17</i>	<i>8</i>
<i>TOTAL GASTRECTOMY</i>	<i>18</i>	<i>8</i>
<i>SUBTOTAL GASTRECTOMY</i>	<i>32</i>	<i>15</i>

in these patients because of the extent of their disease.

Palliative procedures had an operative mortality of 22 percent again similar to that reported in other series (3, 4, 5). However, our 5 percent operative mortality in the curative procedures is lower than that reported in the literature, which varies between 10 percent - 20 percent (5, 7). We think this reflects a better selection of the patients submitted to this type of surgery in our hospital.

The extremely poor results with esophagogastrectomy, exploration and biopsy, and gastrojejunostomy all indicate that there are procedures that have little to offer to the patient with gastric cancer. Esophagogastrectomy should be limited to localized disease in an otherwise good surgical risk patient, being employed only as a curative procedure. Gastrojejunostomy, with a 31 percent operative mortality and a median survival of 4 months, can not be considered as an adequate palliative procedure and we think must be discarded in the surgical management of the patient with gastric cancer. After exploring the patient resection should be attempted whenever possible because this operation offers better palliation than other means of treatment, and as pointed out previously it is often impossible at the time of exploration to determine which resections are for "cure" and which are for "palliation".

The poor results obtained in the surgical treatment of these patients are a direct consequence of the small number coming to therapy with localized disease (13 percent in this series). This has been clearly demonstrated by Japanese workers, which reported

a five-year survival rate of 90 percent after surgical treatment of superficial, early gastric mucosa carcinoma detected by mass radiological or endoscopic screening in non-symptomatic and minimal symptomatic patients (8). Better results in the surgical therapy of gastric carcinoma would be achieved only by earlier diagnosis and not by more radical surgery.

Acknowledgments

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1. Committee on Nutrition: Commentary on breast feeding and infant formulas, including proposed standards for formulas. *Ped* 52:278-285, 1976.

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Smith GR et al: *Psychosomatics* 15:138, 3rd quarter, 1974

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Tobin JM et al: *Geriatrics* 25(6) 122, 1970

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Bernstein JG: *Clinical Psychopharmacology*
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Bernstein JG: *Management of Side Effects Related to Antipsychotic Drug Therapy* An Interview, 1978, p 12

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required. Persistent extrapyramidal reactions have been reported and the drug may have to be discontinued in such cases.

Withdrawal Emergent Neurological Signs: Abrupt discontinuation of short-term antipsychotic therapy is generally uneventful. However, some patients on maintenance treatment experience transient dyskinetic signs after abrupt withdrawal. In certain cases these are indistinguishable from "Persistent Tardive Dyskinesia" except for duration. It is unknown whether gradual withdrawal will reduce the occurrence of these signs, but until further evidence is available haloperidol should be gradually withdrawn.

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Cardiovascular Effects: Tachycardia and hypotension. **Hematologic Effects:** Reports of mild, usually transient leukopenia and leukocytosis, minimal decreases in red blood cell counts, anemia, or a tendency toward lymphomonocytosis; agranulocytosis rarely reported and only in association with other medication.

Liver Effects: Impaired liver function and/or jaundice reported. **Dermatologic Reactions:** Maculopapular and acneiform reactions, isolated cases of photosensitivity, loss of hair.

Endocrine Disorders: Lactation, breast engorgement, mastalgia, menstrual irregularities, gynecomastia, impotence, increased libido, hyperglycemia and hypoglycemia.

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OPERATION BY ALLIED HEALTH PROFESSIONAL PERSONNEL OF A LONG TERM HYPERTENSION DETECTION AND TREATMENT PROGRAM

Elí A. Ramírez, MD, MSc(Med), FACP, Jean M. Da More, RN,
José L. Cianchini, MD and Ana J. Romeu, RN

Summary: Towards the end of 1972, a program was activated at the San Juan Veterans Administration Hospital that systematizes the detection and treatment of hypertension and utilizes primarily allied health professional personnel. At that time it was anticipated that because of unfavorable socio-cultural factors, it might be difficult to implement the program.

The actual experience has been the opposite. The program has been very well received by the clientele of Puerto Rican veterans. In terms of the number of patients examined and treated, the percentage of patients maintained under follow-up and the control of the hypertension, the results have been highly satisfactory. The implementation of this model, operated by allied health professional personnel under minimal physician supervision has improved the utilization of available resources. We believe that this experience may be projected to the application of similar programs elsewhere in Puerto Rico and in other countries with cultural bases similar to ours.

Resumen: A finales del año 1972, se activó en el Hospital de Veteranos de San Juan, un programa que sistematiza la detección y el tratamiento de la hipertensión y utiliza primariamente personal profesional de ciencias aliadas a la salud. En aquel tiempo se anticipó que debido a factores socio-culturales desfavorables, la implantación de dicho programa podría ser difícil.

La experiencia fue completamente opuesta. El programa ha sido muy bien recibido por la clientela de veteranos puertorriqueños. En términos del número de pacientes examinados y tratados, del porcentaje de pacientes mantenidos bajo seguimiento y del control de la hipertensión, los resultados han sido altamente favorables. La implantación de este modelo, operado por personal profesional de ciencias aliadas a la salud bajo mínima supervisión por médicos, ha mejorado la utilización de los recursos disponibles al hospital. Creemos que esta experiencia puede proyectarse hacia la aplicación de programas similares en otras instituciones de Puerto Rico y en otros países con bases culturales parecidas a las nuestras.

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Introduction

The purpose of this presentation is to report the experience at the San Juan Veterans

Administration Hospital with the implementation of a long-term follow-up program for the detection and treatment of hypertension, operated primarily by allied health professional personnel.

This project originally started in 1972 as part of an effort by the Veterans Administration to apply the results of the then recently completed VA Cooperative Studies. A pilot program was developed at 32 Veterans Administration Hospitals. Having been a participant in the VA Cooperative Studies, the San Juan V. A. Hospital was selected to establish one of the pilot clinics.

The members of the Planning Committee for the program were in agreement that in order to enable the detection and treatment of the 10 percent of the veteran population which is estimated to suffer from hypertension, an innovative approach would be necessary. Even with its substantial resources, the Veterans Administration would not be able to recruit enough physicians to take care of this large number of patients. In addition, physicians, by and large would be unwilling to accept long term care of essentially asymptomatic individuals. For these reasons it was decided that allied health professional therapists, under the supervision of physicians would be trained to provide the necessary care.

There were several reasons to anticipate that there might be problems in establishing this model in our hospital:

- 1) In Puerto Rico as in the United States, the citizenship in general has become accustomed to receive medical care only from physicians. Nurses, by and large have practiced their profession within the traditional role, taking care not to appear at any time like physician substitutes. The laws that regulate the

licensing of physicians and nurses, specify clearly the respective responsibilities of the two professions.

- 2) Another issue of concern was that since the clinic would be only for male veterans, it might be cumbersome for female nurses to handle those essential aspects of anti-hypertensive drug treatment related to sexual dysfunction. Up to that time, information exchange of this type between patients and nurses was not customary in our hospital.
- 3) There were no other health care professionals available to provide this service. While several universities in the mainland had already developed physician assistant training programs, our local institutions had not taken any steps in this direction. In fact an attitude of skepticism seemed to prevail in the community regarding the physician substitute model.
- 4) The hospital had had no similar programs before. Traditional physician care was always given by physicians and the patients gave no indication that they wanted any change in this relationship. The perception of this attitude also contributed to the impression that the patient clientele might reject the program that was being planned for them.

Methods

The same clinic protocol was used by all hospitals. Its most important features are as follows:

TABLE I
Treatment Criteria

<i>Average diastolic (5th phase)</i>	<i>104 mm. Hg X 3 - all treated</i>
<i>Average diastolic (5th phase)</i>	<i>90 - 104 mm. Hg:</i>
<i>Male</i>	<i>1</i>
<i>Black</i>	<i>1</i>
<i>Age < 35 years</i>	<i>1</i>
<i>All three diastolics > 94 mm. Hg</i>	<i>1</i>
<i>All three systolics > 164 mm. Hg</i>	<i>1</i>
<i>Severe hypertension father or mother</i>	<i>1</i>
<i>Hyperlipemia or hyperglycemia</i>	<i>1</i>
<i>Target organ damage</i>	<i>2</i>
	<hr/>
	<i>Sum</i>
<i>Ave. diastolic</i>	<i>Treat if sum is</i>
<i>90 - 94</i>	<i>4 or more</i>
<i>95 - 99</i>	<i>3 or more</i>
<i>100 - 104</i>	<i>2 or more</i>

The purpose is to detect the greatest number possible of hypertensive veterans and to offer treatment whenever it is indicated.

The clinics are supervised by a part-time physician but the direct care in more than 90 percent of the cases is given by nurses. The staffing pattern of each clinic consists of two nurses, a nursing assistant and a secretary. The nurses have been trained with particular emphasis on the treatment and follow-up of essential hypertension rather than on the diagnostic and management details of secondary hypertension.

The nurse consults the physician when indicated by the management algorithms, and/or by her own judgment whenever there are circumstances not covered by the protocol.

Basic historical and demographic data are obtained at the screening interview. Three blood pressures are determined in the sitting position in the right arm, using a mercury sphygmomanometer. All patients with an average fifth phase Korotkoff diastolic pressure over 105 mm. Hg receive an appointment for a more detailed evaluation. Those with a diastolic

pressure between 90 and 105 mm Hg who are less than thirty-five years of age or who are black also receive an appointment for evaluation. Those individuals not selected for evaluation receive appointments for follow-up visits at intervals determined by the level of their blood pressure.

At the evaluation visit a detailed history and physical examination are performed. The recommendations of the National Joint Committee on the Detection, Evaluation and Treatment of Hypertension are followed with respect to evaluation of cardiovascular-renal-function through laboratory examinations (1). A simple schedule, shown in Table I is used to determine the initial treatment on the basis of the blood pressure level, age, race, presence of cardiovascular risk factors, history of hypertension in the family, and evidence of previous damage to the brain, heart and kidneys (2). Patients with diastolic pressures over 140 mm. Hg. are hospitalized immediately for treatment.

The treatment schedule is based on the step care scheme recommended by the working group of the Advisory Committee on Education on Hypertension of the Department of Health, Education and Welfare of the United States (3). The scheme may be modified by the supervisory physician in accordance with his best clinical judgment.

The goal of treatment is an average diastolic pressure less than 90 mm. Hg in the sitting position. If the patient is compliant and the blood pressure is not controlled to less than 100 mm. Hg without adverse secondary effects, the patient is referred for additional investigation and/or treatment.

Results

Between the start of the clinic late in 1972 until September 1978, 20,459 individuals were screened for hypertension. Of these, 6,570 (32.1 percent) had a screening diastolic pressure over 90 mm. Hg.

The percentage of hypertensives detected at any one period has varied inversely according to the number of subjects screened. This is due probably to a constant influx of known

hypertensives who want to have their blood pressure checked, and represent a greater proportion of the screenees whenever the detection activity is relatively small.

The total number of visits for treatment since 1972 to September 1978 was 12,750. The number of monthly visits has increased progressively reaching 330 in September 1978. The number of patients under treatment also has increased progressively and at the same date it was 871.*

A retrospective study of 239 patients who were on treatment in October of 1974 was done in order to determine the overall performance of the clinic. During the following two years, 36 were lost to follow-up for several reasons: 2 were referred to private physicians, 17 were referred to other clinics in the hospital because they had other serious conditions, 3 moved and could not return to the clinic, 2 died (one due to a car accident and one due to a myocardial infarction), and 12 did not return to the clinic for unknown reasons. At the end of two years there were 203 patients remaining under follow-up, representing 85 percent of the original number.

The distributions of diastolic blood pressures of these 203 patients when they started treatment and 2 years later are shown in Table II. When they started treatment, seventy (34 percent) were between 91 and 104 mm. Hg, 95 (47 percent) between 105 and 114 mm. Hg, and 38 (19 percent) above 114 mm. Hg. Two years later, 128 (63 percent) were less than 91 mm. Hg, 66 (33 percent) between 91 and 104 mm. Hg, 9 (4 percent) between 105 and 114 mm. Hg, and none were over 114 mm. Hg. These figures indicate that almost 2/3 reached the goal of a diastolic pressure

* - In January 1980, the number of visits was 426 and the number of patients under follow-up was 1112.

TABLE II

Distribution Diastolic Pressures

<i>mm. Hg</i>	<i>Initial</i>	<i>After 2 years Rx</i>
< 91	0	128 (63 percent)
91 - 104	70 (34 percent)	66 (33 percent)
105 - 114	95 (47 percent)	9 (4 percent)
> 114	38 (19 percent)	0

TABLE III

Frequency of Therapeutic Regimens

<i>Diuretic alone</i>	113
<i>Diuretic + AMDopa</i>	48
<i>Diuretic + Reserpine</i>	12
<i>Diuretic + Hydralazine</i>	6
<i>Diuretic + Clonidine</i>	6
<i>Diuretic + Guanethidine</i>	4
<i>Diuretic + Hydralazine + Propranolol</i>	6
<i>Diuretic + Hydralazine + AMDopa</i>	4
<i>Diuretic + AMDopa + Clonidine</i>	1
<i>Diuretic + Reserpine + Hydralazine</i>	1
<i>No medication</i>	2

203

of 90 mm. Hg.

The average age of the group was 49.7 years upon starting treatment. The patients had experienced a considerable number of hypertensive complications before starting treat-

ment. Seven (3 percent) had had a cerebral accident, twenty-six (11 percent) had evidence of coronary disease, twenty-six (11 percent) had other evidence of cardiac disease such as congestive heart failure and electrocardiogra-

TABLE IV
Comparison SJVAH and Overall Program
(Oct. 1978)

	Overall Program	SJVAH
<i>Screened</i>	500,000	20,459
> 90 mm. Hg	29 percent	32.1 percent
<i>Treated</i>	25,000	871 (active)
≤90 mm.Hg.	53 percent	63 percent
<i>Follow-up</i>	62 percent (2.5 yrs.)	79 percent (4 yrs.)

phic abnormalities, and five (2 percent) had grade III hypertensive retinopathy. In addition, fourteen (6 percent) had a diagnosis of gout and forty-nine (21 percent) were diabetics.

During the two years of follow-up one patient had a cerebral accident, seven developed new angina, and seven had new manifestations of cardiac disease. In addition, five developed gout and ten developed diabetes. No relationship was noted between the appearance of new events and the degree of control of blood pressure.

The regimens prescribed in the clinic are shown in Table III. Over half of the patients were treated with a diuretic alone. Approximately 1/3 were treated with a diuretic and another drug, most frequently alphamethyldopa and then reserpine; only 6 percent required three drugs. In October 1978, the patients of this group who remained under

treatment were re-studied. The relative proportions of drug combinations in use remained more or less the same except that propranolol had largely displaced alphamethyldopa as a second drug. It must be noted that during the last two years only fifteen additional patients were lost to follow-up; that is, the percentage under follow-up of the original group was 79 percent after four years of treatment.

Discussion

A comparison between these figures and those from the other 32 hospitals of the Veterans Administration where this program has been established is shown in Table IV (4). In all hospitals, a total of approximately 500,000 individuals have been examined and the percentage of individuals with screening diastolic pressures above 90 mm. Hg is 29 percent com-

pared with ours of 32.1 percent. 25,000 patients have been put under treatment in the total program of whom 53 percent are controlled with a diastolic pressure less than 90 mm. Hg; in our clinic the corresponding percentage is 63 percent. In the overall program, 62 percent of the initial group remained under treatment after 2 1/2 years of follow-up; in our clinic 79 percent remain under follow-up after four years.

The difficulties that were anticipated upon implementing this program in our hospital have not materialized. The nurse therapists have been extremely well accepted in the clinic. This is evidenced by the high recruitment rate and percentage of follow-up which compare favorably with those of the other clinics in the hospital and of the other clinics of this program in other VA hospitals. With respect to the control of hypertension, the results also compare favorably with those of the other hospitals.

The implementation of this model, operated by allied health professional personnel under minimal physician supervision, has improved the utilization of the available resources at our hospital. This approach offers a practical and economical solution to the public

and personal health problem that hypertension represents. It enables the effective detection and treatment of a large number of asymptomatic hypertensives at reasonable cost, and should secure for the population at risk the benefits of anti-hypertensive therapy. We believe that this experience encourages the application of similar programs elsewhere in Puerto Rico and in other countries with cultural bases similar to ours.

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CONTESTACIONES A MEDI-QUIZ:

1. e)
2. d)
3. a), b) y c)
4. c)
5. b)
6. a), b), c) y d)

ESOPHAGEAL ATRESIA AND TRACHEOESOPHAGEAL FISTULA: A TEN YEAR REVIEW AT THE UNIVERSITY HOSPITAL

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Summary: Esophagel atresia with or without tracheoesophageal fistula is one of the classic congenital deformities in pediatric surgery. There has been a fairly constant incidence of 1.6 cases per 10,000 births in the U. S. over the past 10 years. In Puerto Rico where there is an average of approximately 70,000 yearly births, one would expect 11 cases of this deformity per year, assuming a similar rate. We have reviewed the cases of this condition seen at the University and the University Children's Hospitals for the 10 yr. period of Jan 1968-June 1978. Forty seven cases were identified, for a yearly incidence of 4.7. Information from records were obtained for 41 of these. Of those reviewed: a) There was a 58 percent male predominance; b) Seventy five percent were of type C, 21 percent type A, 4 percent type E; c) 26 percent were born at the University Hospital and 74 percent were referred from other institutions; d) the common signs and symptoms were excessive salivation, respiratory distress, pneumonia and "vomiting"; e) the diagnosis could routinely be made by failure to pass a nasogastric tube and by chest

x-ray; f) there were associated anomalies in 40 percent of type A, 28 percent of type C cases, the most common being imperforate anus and cardiovascular anomalies; g) there was an overall gross mortality rate of 51 percent, some succumbing before surgical interventions, others after.

Resumen: Atresia de esófago con o sin fístula traqueoesofágica es un complejo clásico de deformidades congénitas dentro del campo de la cirugía pediátrica. En Estados Unidos se reporta una incidencia relativamente constante de 1.6 casos por 10,000 nacimientos. Asumiendo una tasa similar, en Puerto Rico donde ocurren aproximadamente 70,000 nacimientos anuales, esperaríamos 11 nuevos casos de esta anomalía por año. Hemos revisado los casos de esta condición tratados en los Hospitales Universitario e Universitario de Niños durante el período de enero 1968 a junio 1978. Cuarenta y siete casos fueron identificados, una incidencia anual de 4.7. Se obtuvo información de los expedientes de 41 de estos. De los casos revisados encontramos: a) Una frecuencia de varones de 58 por ciento; b) 75 por ciento presentaban el tipo C, 21 por ciento el tipo A y 4 por ciento el tipo E; c) 26 por ciento nacieron en el Hospital Universitario y 74 por ciento fueron referidos de otras instituciones; d) Los síntomas

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TABLE I

Esophageal Atresia: Presenting Signs and Symptoms

	No.
<i>Excessive Salivation</i>	22
<i>Respiratory Distress</i>	14
<i>Pneumonia</i>	8
<i>"Vomiting"</i>	5
<i>Polyhydramnios</i>	1
<i>Asymptomatic</i>	5

TABLE II

Esophageal Atresia: Diagnostic Tests

	No.
<i>Nasogastric Tube</i>	32
<i>Chest X-Ray</i>	32
<i>Contrast Study</i>	5

TABLE III

Esophageal Atresia: Age at Diagnosis

	No.	Percent
<i>< 24 hours</i>	16	39
<i>24-72 hours</i>	18	44
<i>> 72 hours</i>	3	7
<i>Undetermined</i>	4	10

y signos más comunes fueron salivación excesiva, angustia respiratoria, pulmonía y "vómitos"; e) El diagnóstico se pudo hacer rutinariamente al no poder introducir un tubo nasogástrico y con la placa de pecho; f) Se

encontraron anomalías asociadas en 40 por ciento del tipo A, 28 por ciento del tipo C; las más comunes fueron ano imperforado y anomalías cardiovasculares; g) La mortalidad total para este grupo de infantes fue de 51

por ciento, algunos muriendo antes y otros después de una intervención quirúrgica.

Esophageal atresia, with or without tracheoesophageal fistula is an important congenital malformation in the field of pediatric surgery. National statistics in the U. S. show a relatively constant incidence over the past 10 years of 1.6 cases per 10,000 births (1). We do not have a similar registry in Puerto Rico to determine the incidence of this anomaly here. However, if we apply the same incidence rate to our yearly births, we estimate that approximately 11 cases per year should be seen.

There are several institutional series reported (2, 3, 4), and a cooperative multi-institutional report (5) defining the clinical picture, treatment and results obtained in this condition. In an effort to define these parameters in our institution, we undertook the following retrospective review of esophageal atresia and tracheoesophageal fistula at the University and University Children's Hospital.

Method

An attempt was made to obtain all records with the diagnosis of esophageal atresia and/or tracheoesophageal fistula for the period of January 1968 to June 1978. The majority of the records were obtained through the diagnostic codes at the Record department of the University Hospital. Other partial records and summaries were obtained by reviewing the monthly statistics reports of the nursery at the University Children's Hospital. A total of 47 cases were identified by diagnosis during this period. Forty one records were obtained; 23 were complete, and 18 partial. The information in these records forms the basis for this communication.

Results

Incidence, Birthplace and Sex Distribution - Figure 1

During the study period there were a total of 47 cases treated at our institution for an annual incidence of 4.7. Of those reviewed, approximately one fourth were born in this institution and the remainder were referred from other areas: 8 percent Metropolitan San Juan, 56 percent rest of the island, and 8 percent outside Puerto Rico. Fifty eight percent were male, 42 percent female.

Presenting Signs and Symptoms (Table I)

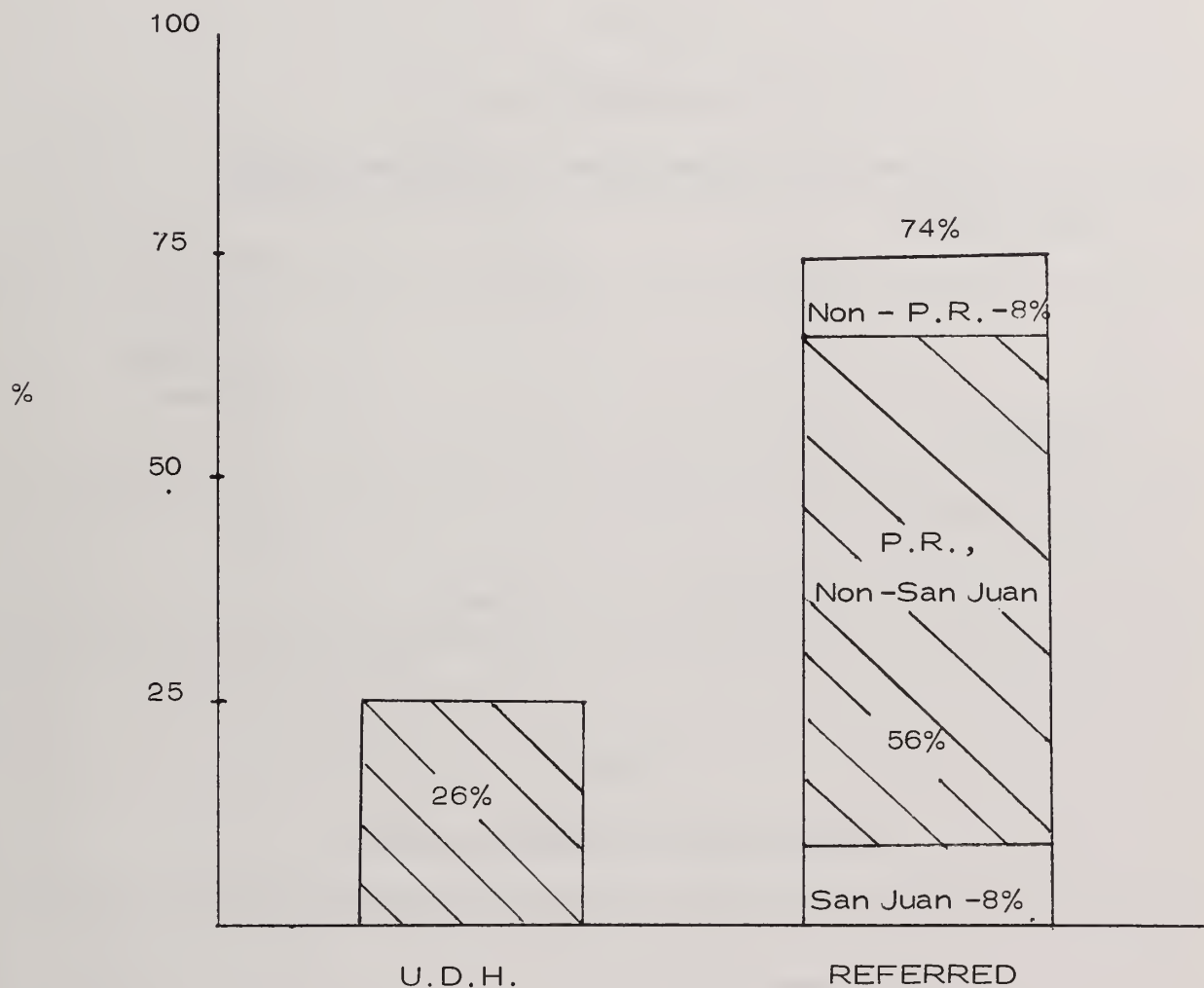
Excessive salivation, respiratory distress and pneumonia were the major presenting problems. It is of interest that there were 5 cases (12 percent) in which the diagnosis was made before symptoms developed, by routine passage of a nasogastric tube.

Diagnosis Tests and Age at Diagnosis (Tables II, III)

The diagnosis was confirmed in most cases by passage of a nasogastric tube and/or by plain chest X-Ray. In a few cases a contrast study was utilized. The diagnosis was confirmed within 24 hrs. in 39 percent and from 24 to 72 hrs. in 44 percent.

Types and Associated Anomalies (Tables IV, V)

The types were allocated using Gross' Classification (6). Of the cases that could be classified from information in the records, 21 percent were type A (esophageal atresia without fistula), 75 percent were type C (esophageal atresia with fistula to lower segment



INCIDENCE OF CASES, U.D.H. = 4.7 PER YEAR

Figure 1: Place of Birth

and 4 percent were type E (fistula without atresia). We found no cases of types B (fistula to upper segment) or type D (fistula to both upper and lower segments).

There were other associated anomalies in 34 percent of the cases. Most of these were related to the gastrointestinal and cardiovascular systems (Table V).

Surgical Procedures (Table VI)

The procedures varied with the type of atresia. For the common type C, the most frequently utilized approach involved division of the fistula, primary repair with end to end anastomosis, and gastrostomy, all in the newborn period. In type A atresia, a temporary cervical esophagostomy for drainage of the upper pouch, followed by delayed colon interposition was most frequently performed.

TABLE IV

Esophageal Atresia: Types of Atresia and Associated Anomalies

<i>Type \ Anomalies</i>	<i>Present</i>	<i>Absent</i>	<i>Total Type</i>
<i>A</i>	2	3	5 (21 percent)
<i>C</i>	5	13	18 (75 percent)
<i>E</i>	1	--	1 (4 percent)
<i>Undetermined</i>	6	11	17
<i>TOTAL ANOMALIES</i>	14	27	41
	(34 percent)	(66 percent)	

TABLE V

Esophageal Atresia: Associated Anomalies

<i>Gastrointestinal</i>	8
<i>Imperforate Anus</i> — 6	
<i>Duodenal Atresia</i> — 1	
<i>Annular Pancreas</i> — 1	
<i>Cardiovascular</i>	4
<i>C. N. S.</i>	2
<i>Skeletal</i>	2
<i>Renal</i>	1
<i>Down's Syndrome</i>	3
<i>Others</i>	3

TABLE VI

Esophageal Atresia: Surgical Procedures			
Procedure	Type	A	C
C. E. + G. Late C. I.		3	--
C. E. + G. Late S. T.		1	--
C. E. + G.		1	--
D. T. E. + C. E. + G. Late C. I.		--	2
D. T. E. + C. E. + G.		--	1
D. T. E. + P. R. + G.		--	13
D. T. E. + P. R.		--	2
TOTAL		5	18

Legend:

- C. E. - Cervical Esophagostomy
- C. I. - Colon Interposition
- D. T. E. - Division Tracheoesophageal Fistula
- G. - Gastrostomy
- P. R. - Primary Repair
- S. T. - Stomach Translocation

Mortality (Tables VII, VIII, IX)

The mortality varied with the type of surgical intervention. Infants who underwent primary repair in the neonatal period had a mortality of 36 percent; those who had decompressive esophagostomy and gas-

trostomy 60 percent; and those with delayed colon interposition 20 percent. Those cases that did not have surgical intervention had a 100 percent mortality (Table VII).

When we look at mortality and birth weight we find a definite relation: 79 percent mortality in those under 2.5 kg, 45 percent

TABLE VII

Esophageal Atresia: Mortality Related to Procedures

	No. Cases	Deaths	Mortality
<i>Primary Repairs</i>	22	8	36 percent
<i>Gastrostomy & Esophagostomy</i>	5	3	60 percent
<i>Late Colon Interposition</i>	5	1	20 percent

TABLE VIII

Esophageal Atresia: Relation of Birth Weight to Survival

WT (KG)	Survived	Dead
1.5 - 2.5	3	11
2.5 - 3.5	6	5
> 3.5	--	--
Undet. Wt.	11	5
TOTAL	20 (49 percent)	21 (51 percent)

TABLE IX

Esophageal Atresia: Contributing Causes of Death

Cause	1 st Procedures (n = 13)	No Procedures (n = 4)
<i>Respiratory</i>	9	3
<i>Sepsis</i>	10	2
<i>Wound Dehiscence</i>	3	--
<i>Esophageal Disruption</i>	2	--
<i>Renal</i>	1	1
<i>Undetermined</i>	3	--

in those over that weight. The statistical significance is borderline by the Chi-Square test $p < 0.1$ but $p > 0.05$. (Table VIII). The overall mortality was 51 percent.

The principal cause of death were respiratory and septic complications. These were followed by technical surgical problems of wound dehiscence or esophageal disruption (Table IX).

Discussion

Esophageal atresia and tracheoesophageal fistula is a complex of embryologically explainable anomalies, although no one factor has been identified as etiologic. Its incidence appears to be relatively constant, at approximately 1.6 cases per 100,000 births (1). This rate is similar in the U. S. (as reported by Haight) and in Australia (by Myers) (7). In Puerto Rico, the actual rate of incidence has not been determined since there is no registry for this congenital anomaly. If one applies the U. S. rate to our yearly births, we would expect approximately 11 cases per year. Our series reviews an average of 4.7 cases per year treated at the University Hospital.

Gross classified the major types of this congenital malformation (6). The distribution of these appears remarkably constant throughout several reported series (1, 2, 3, 4). Type C, esophageal atresia with a distal tracheoesophageal fistula, is by far the most commonly encountered. This is followed by types A, (pure atresia) and E, (pure fistula) seen in approximately 10 percent and 5 percent respectively. Types B, D are exceedingly rare, usually reported in less than 1 percent of cases. Our series distribution conforms roughly to this pattern.

Associated anomalies are found in a significant percentage of cases. We noted a 34 percent incidence, which correlates well

with that reported in various other series (3, 4, 7). The American Academy of Pediatrics study suggests a higher incidence of 52 percent (5). The major anomalies are found in the gastrointestinal and cardiovascular systems. Of interest is the conglomeration of anomalies that has been grouped into the "Vacter Syndrome": V-Vertebral, A-Anus (imperforate), C-Cardiac; T. E. - Tracheoesophageal, R-Renal. These anomalies occur together in a significant number of cases, and therefore it is important to look for others when one or more are initially noted clinically.

The presenting clinical picture is predictable from the nature of the anomalies. Symptoms generally are related to inability to swallow ("vomiting", unable to swallow, unable to pass a tube) or to secondary pulmonary complications from aspiration and/or reflux through the fistula (respiratory distress, cyanosis, pneumonia). These suggestive signs are noted at various times after birth, but there is a group of 10-20 percent in which this is not recognized and not diagnosed during the first 72 hrs. (4). If routine attempts at passage of a nasogastric tube were carried out, all these cases could be diagnosed at birth (except for type E cases). This maneuver was carried out in 12 percent of cases and in a similar fraction in other reports (5). Polyhydramnios is a sign that should alert us to the possibility of esophageal atresia (7), but in our reviewed cases, this was recorded in only one case.

The diagnosis can be arrived at quite simply by failure of the attempted passage of a nasogastric tube, and a chest X-ray. The X-ray will typically show the catheter looped in the blind upper pouch. In our cases this was the method by which the condition was most commonly diagnosed. The use of contrast material to fill the upper pouch is not usually necessary, and except when done under fluoroscopic control and with bronchographic

dye, not indicated. If one discards the very rare types B and D, one can readily determine whether one is dealing with a type A or C anomaly by observing on the X-ray whether or not gas is present in the abdominal gastrointestinal tract.

Management of these infants varies with several factors: gestational age, birth weight, type of atresia - fistula, associated anomalies, and acquired respiratory problems. For the usual type of anomaly with an atresia and a distal fistula, if there are no complicating factors, the procedure of choice is division of the fistula with a primary end to end esophago-esophagostomy and gastrostomy. We found this to be the most common approach at the University Hospital. There are several technical variations of this approach that can be used but our group of cases was too small to allow us to determine if there was any advantage associated with one or another.

For the second most common situation (type A) the usual approach was a delayed esophagoplasty using colon as a conduit, because the atretic gap is usually too long to allow for primary repair. There is recent interest in the use of esophageal myotomies in an attempt to perform a primary repair in the neonatal period, using only esophageal segments in these cases of long segment atresia (8).

Survival is also related to various factors including birth weight, type of atresia, presence of associated anomalies, and presence of pneumonia. It is also a function of the improved management techniques developed for the sick neonate in more recent years. Typical figures for overall survival in different time periods are those reported by The Royal Children's Hospital Melbourne: 31 percent for 1948-52, 60 percent for 1953-57, 55 percent for 1958-62, 81 percent for 1963-67, 89 percent for 1968-72, 86 percent for 1973-77 (7). We found a survival for the cases reviewed at the University Hospital of 49 percent. A five

year review of cases operated by members of the Surgical Section of the American Academy of Pediatrics during 1958-62 revealed a 61 percent gross survival rate (5).

It is clear that in addition to the changes in the care of these infants, the intrinsic condition of the neonate is important. Waterston has proposed a clinical classification scheme according to risk factors (7). He found a progressive decrease in survival with poor risk groups: 92 percent survival for those more than 2.5 kg and well (A), 71 percent for those with weights between 1.8 and 2.5 kg or with moderate pneumonia and/or other anomalies (B), and 38 percent for those less than 1.8 kg or with severe pneumonia or anomalies (C). Using the same classification the most recent experience (1973-77) at the Royal Children's Hospital, Melbourne reports survival of 100 percent for class A, 84 percent for class B and 75 percent for class C (7). Although we did not classify our cases using this method, it is clear from our review that birth weight did indeed influence survival, being 55 percent in those over 2.5 kg and only 21 percent in those under that weight.

Now that survival can be achieved with significant regularity, there is considerable interest in the long term results in these children. Due to the fragmentary nature of the follow-up in our cases, we were not able to clearly document the long term course in the survivors. However, stricture developed in 9 of 13 children who had primary repair. This complication was reported in 39 percent of the American Academy of Pediatrics study (5). Dysphagia may be related to stricture, but can be due to esophageal dysmotility, which is present even before surgical intervention (7). Respiratory complications of bronchitis, and pneumonia are also more common in this group of children. Both of these problems however appear to become less important as the length

of follow-up becomes longer (7).

Acknowledgments

All these cases were managed by various attending physicians in the Departments of Surgery and Pediatrics of the University of Puerto Rico School of Medicine. We appreciate the excellent secretarial assistance of Mrs. Laura Mercado de Díaz.

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CONTESTACIONES A MEDI-QUIZ

1. False
2. True
3. False
4. True
5. False
6. False
7. True
8. False
9. True
10. False
11. True
12. False

LEARNING PRIMARY CARE IN A PRIMARY CARE SETTING

José Ramírez Rivera, MD and Miguel H. del Toro, MD

As recently as three years ago, the Rincón Health Center had not laboratory or X-ray facilities. It provided symptomatic care to a population estimated at 10,000 with one fully licensed and one partially licensed practitioner assigned by the Puerto Rico Department of Health. In July 1975, a rural health initiative grant of \$280,000 was obtained from the Department of Health, Education and Welfare to help develop a self-sustained primary care facility. Subsequent yearly grants have made possible a dramatic improvement of the old Department of Health facilities and the services provided. An effective diagnostic and treatment center with appropriate laboratory and X-ray services and a functional emergency room service 24 hours a day has been established. The center has progressively become the teaching ground for medical and nursing students and a source of orientation for premedical students and allied health personnel. In this article we review some of the methods used to develop the professional aspects of this teaching primary care facility and detail the rewarding experience of a fourth year medical student who kept a careful diary of her patient encounters during her two month rotation.

From the Rincón Rural Health Initiative Project, Department of Medicine, Mayaguez Medical Center, Mayaguez, P. R.

Presented in part at the Regional Meeting of the American College of Physicians, Ponce, Puerto Rico, October 7, 1977.

Methods

With salaries at the level of \$27,000, plus \$5,000 estimated in fringe benefits, two young physicians were persuaded to leave the protective walls of the Mayaguez Medical Center and become pioneers in primary health care. One had two years of training in internal medicine, the other had three years of post-graduate experience in surgery. Neither had had formal training in primary medicine. They knew the name and *were willing to learn* the rules of the primary care game.

By the end of the first year, the heat of the medical audits and the pressures of following a problem oriented record had led the two physicians assigned to Rincón by the Commonwealth to seek reassignment elsewhere. The skills, knowledge and attitudes learned in an unapproved AMA internship had not prepared them for this experience (1). We were then authorized to recruit two interns finishing at the Medical Center at Mayaguez. These two, although not specifically oriented in primary care medicine, had at least a sound background in clinical diagnosis and treatment.

Physicians worked from 50 to 60 hours a week. They dedicated one morning or afternoon once a week to maintaining their knowledge and to develop new skills by joining the on-going specialty clinics of their choice at the Mayaguez Medical Center. The visit to the Medical Center also served to keep in touch with the clinical course of the few patients previously referred there. A weekly medical audit of 10 percent of patients records stripped bare ineffective clinical management, protocols and mature judgments sought to settle differences of opinion improved medical knowledge and the quality of care. The weekly tutorial session with a certified radiologist of one of the physicians, where puzzling gastrointestinal series



Fig. 1: Sideview of Rincón diagnostic and treatment.

and questionable lesions in intravenous pyelograms were viewed, and the necessity to share the enlightenment obtained with expectant colleagues at the Health Center, helped measurably to develop the essential clinical skills of these young physicians.

But interest in patients was not limited to those seeking help at our door. That would not be good primary care.

Vaccination programs were successfully launched in neighborhoods seriously deprived of medical orientation. All willing Rincon's school children had the mandated school examinations. Successful forays were also made into nearby industries to uncover and improve the health of workers with surprising results (2).

Into this evolving setting, Harvard University School of Medicine sent one female senior medical

student for her scheduled two months rotation. The first entry in her diary reads:

"I am in a township approximately six miles long by three miles wide, 30 minutes from the Mayaguez Medical Center; 85 percent of the population is unemployed and subsisting on Welfare.

A well groomed health center is at the entrance of the town (Figure 1). This is a town of 5 churches of various sects, one Post Office, two bars, two pharmacies, and various small shops. Fifty to 200 patients are seen daily. Parecenteses and bone marrow aspirations are done and biopsy material is analyzed at the supporting Regional Hospital."

Many of the general impressions of this medical student appeared in the Alumni Magazine of her prestigious University in an appealing article entitled *One Corner* (3). We present here a brief summary of

TABLE I

Distribution by age of 377 patients seen by a medical student in two months:

Age	0-2	2-5	5-10	10-20	20-30	30-40	40-50	50-60	60-70	70-80	80
No. of Patients	37	46	42	57	41	51	18	27	29	20	9

TABLE II

Variety of gastrointestinal, genitourinary and psychiatric disorders seen in a two-month student rotation at Rincón

Gastrointestinal (54):	<i>vomiting and diarrhea 18; constipation 13; abdominal pain 13; ulcer 5; gall bladder 3; pyloric stenosis 1; giardia 1.</i>
Genitourinary (21):	<i>urinary tract infection 20; vaginitis 8; pregnancy (N1) 7; B P H 3; menorrhagia 2; dyspareunia 2; pseudocyesis 2; ectopic pregnancy 1; inevit. abort. 1; coil out 1; orchitis 4; phimosis 1.</i>
Psychiatry (59):	<i>headache 12; "chorro" 12; anxiety 10; obesity 10; depression 8; neurosis 3; dementia 2; alcohol 2.</i>

the nature and extent of her patient encounters.

Observations

Yeou-Cheng Ma saw 377 patients in two months. She was the first encounter medical provider for about half of them. Patients were of all ages (Table I). There were 37 children less than 2 years old, and nine patients above the age 80. She saw a

wide variety of common clinical disorders. She evaluated twenty-four patients with back pain and osteoarthritis, 10 patients with hypertension, six with congestive heart failure and five with angina pectoris. She examined five patients with tinea versicolor, five with an ill-defined dermatitis, and one with psoriasis. She treated 43 patients with ear, nose and throat disorders. She helped treat 20 patients with diabetes mellitus and shared the diagnostic evaluation of one with hyperthyroidism. She diagnosed and drafted ferrous sul-



Fig. 2: Nurse taking the vital signs in screening area of emergency room.

phate prescriptions for thirteen females with iron deficiency anemia; and was overjoyed to recognize, and not treat, one transient fever and lymphadenopathy — cat scratch disease.

Gastrointestinal disorders, ranging from ordinary vomiting and diarrhea to pyloric stenosis of infancy (Table II) trundled through her examining-room door. She planned treatment for 20 patients with urinary tract infections, but saw other genitourinary problems as varied as vaginitis and pseudocyesis (Table II). Yeou-Chen Ma shared with the adventuresome ex-internal medicine resident and three other young physicians, the management of 43 simple upper respiratory infections and nine radiographically demonstrated bronchopneumonias. In the simple, attractive and adequately stocked emergency room,

(Fig. 2) she helped the surgeon turned generalist treat 13 simple fractures, and faced, in some measure, forty-seven other forms of trauma (Table III).

The fifty-nine patients with psychiatric symptoms provided her with a more reliable perception of man than reading two-hundred pages of a psychiatric text (Table II). The differential diagnosis of the colorful "chorro", meaning a vague sensation of chill or heat running up and down the body, was as instructive as was the management of patients with dementia and chronic alcoholism without psychiatrists and without protective iron bars. Only 1 percent of the patients she saw were referred to the Medical Center for evaluation or treatment and 80 percent of the laboratory studies were performed right at the Center in Rincón.

TABLE III

Traumatology seen by a fourth year medical student during a two-month rotation

<i>Foreign bodies</i>	8
<i>Lacerations</i>	7
<i>Infected lacerations</i>	15
<i>Abrasions</i>	9
<i>Head contusions</i>	5
<i>Dog bites</i>	3

Comments

Besides seeing cases and illnesses, this medical student participated in improving the health care and the social behavior of people willing to be guided but not knowing where to go. She saw people with little or no knowledge about health, whose reliance on pills and shots had been fostered by inadequately trained physicians, their only source of medicine and wisdom. She faced young parents in conflict with the newly-found knowledge that the common cold is treated with aspirin and liquids and not with daily injections of Lin-cocin. She learned to overcome the reluctance of humble folk to undergo a physical examination before receiving a prescription. To some of them contact with a physician meant a brief question and a rapidly scribbled note with a number, the number of one of the few bottles in the pharmacy with some medicine still left on it. She perceived the use of home care for incapacitated people of all ages — care we are providing only to the elderly at present because it is paid with Federal dollars. Yeou-Cheng Ma shared our conclusions: Since health is a responsibility heavily influenced by personal behaviour, one of the fundamental functions of any Health Center is the health education of the community.

Conclusion

Primary medicine may be learned in sophisticated University or Community Hospitals if special units oriented to the care of families and community needs are developed, but this is expensive and has the artificiality of all things contrived. In a natural primary care setting the student will deal with the more common diseases, will develop self-confidence by successfully acting as a primary physician, and, perhaps most importantly, will become acquainted, first-hand, with the prevalent medical and social problems of his day. Medical students and young physicians can best learn to recognize and solve the health care needs of Puerto Rico by being a functional part of *properly structured* primary health care centers in our small towns.

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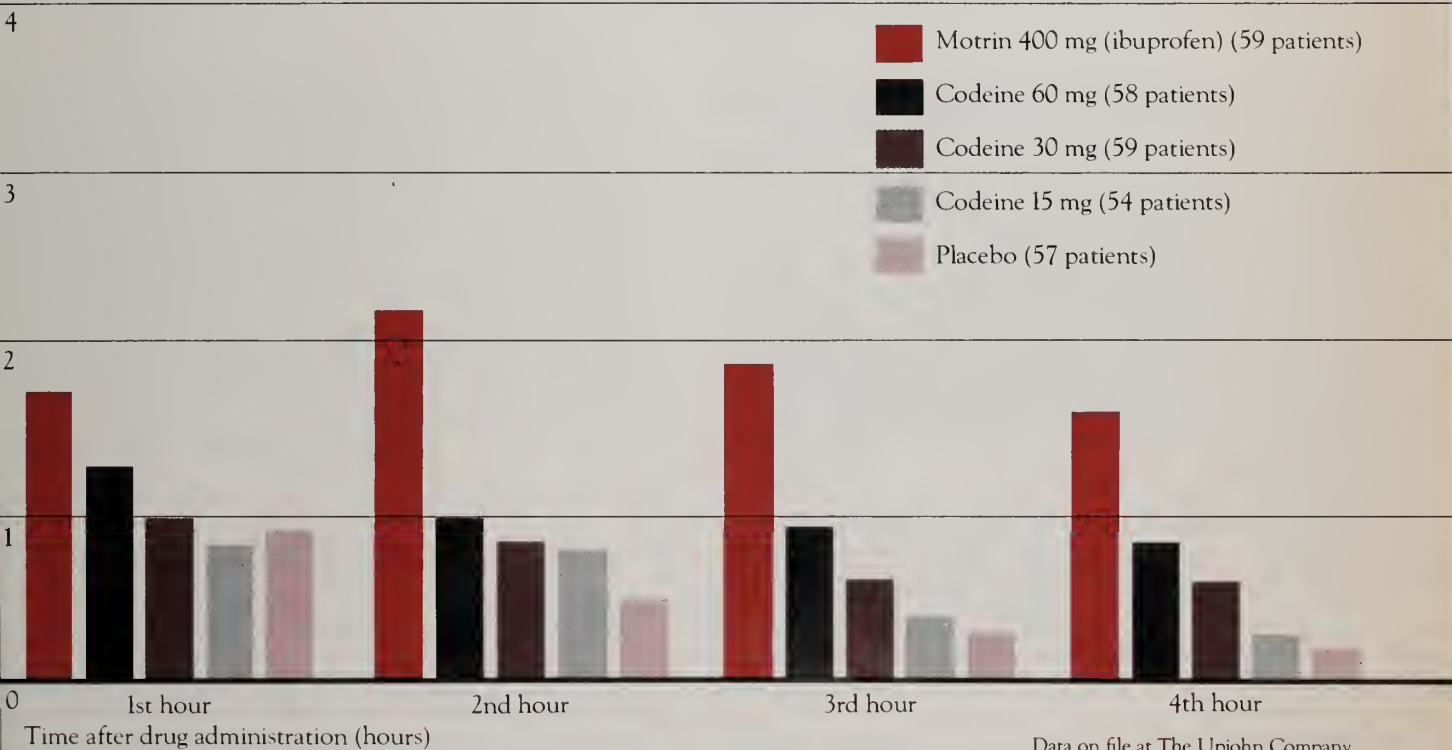
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Peptic ulceration and gastrointestinal bleeding, sometimes severe, have been reported. Ulceration, perforation, and bleeding may end fatally. An association has not been established. Motrin should be given under close supervision to patients with a history of upper gastrointestinal tract disease, only after consulting ADVERSE REACTIONS.

In patients with active peptic ulcer and active rheumatoid arthritis, nonulcerogenic drugs, such as gold, should be tried. If Motrin must be given, the patient should be under close supervision for signs of ulcer perforation or gastrointestinal bleeding.

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*Incidence 3% to 9%.

Incidence less than 1 in 100

Gastrointestinal: Upper GI ulcer with bleeding and/or perforation, hemorrhage, melena. **Central Nervous System:** Depression, insomnia. **Dermatologic:** Vesiculobullous eruptions, urticaria, erythema multiforme. **Cardiovascular:** Congestive heart failure in patients with marginal cardiac function, elevated blood pressure. **Special Senses:** Amblyopia (see PRECAUTIONS). **Hematologic:** Leukopenia, decreased hemoglobin and hematocrit.

Causal relationship unknown

Gastrointestinal: Hepatitis, jaundice, abnormal liver function. **Central Nervous System:** Paresthesias, hallucinations, dream abnormalities. **Dermatologic:** Alopecia, Stevens-Johnson syndrome. **Special Senses:** Conjunctivitis, diplopia, optic neuritis. **Hematologic:** Hemolytic anemia, thrombocytopenia, granulocytopenia, bleeding episodes. **Allergic:** Fever, serum sickness, lupus erythematosus syndrome. **Endocrine:** Gynecomastia, hypoglycemia. **Cardiovascular:** Arrhythmias. **Renal:** Decreased creatinine clearance, polyuria, azotemia.

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ABDOMINAL HEART TRANSPLANTATION THE SEARCH FOR AN ALLOGRAFT EXTRATHORACIC PUMP PRELIMINARY OBSERVATIONS

Luis H. Toledo-Pereyra, MD, PhD, Fernando M. Jara, MD and
Donald J. Magilligan, MD

Summary: Eight abdominal heart transplantation models were tested to determine the most feasible model to function as an extra-thoracic pump. Only models 7 and 8 with anastomoses of the aorta to aorta, pulmonary artery to inferior vena cava, and a dacron graft interposition from the mitral annulus to the aorta (Model No.7) or having an aortic arterial homograft from aorta to left atrium with a gradual occluding clamp (Model No. 8) gave good hemodynamic support.

Resumen: Este trabajo estudia en una forma preliminar ocho diferentes técnicas de trasplante de corazón extratorácico. Las técnicas que dieron mejores valores hemodinámicos y que funcionaron como una bomba cardíaca auxiliar fueron las técnicas siete y ocho. Estas técnicas consistieron en anastomosis de la aorta a la aorta, de la arteria pulmonar a la vena cava y de la aorta a la válvula mitral a través de un injerto de dacrón (Modelo Núm. 7) o de la

aorta a la aurícula izquierda a través de un homoinjerto aórtico arterial (Modelo Núm. 8).

We have been interested in developing a functional abdominal heart transplantation model. However, our results have, in general, been unsatisfactory in particular when the extrathoracic abdominal hearts have been used to support the entire circulation. This work examines eight different heart transplantation models in our laboratories to determine the best available technique that would allow for complete support of the circulation.

Materials and Methods

Donor hearts obtained from adult mongrel dogs were implanted into the abdominal vessels of the recipient animal. After excision, the donor heart was flushed through the aorta with 300-500 ml of Ringer's lactate at 4° C containing 10,000 units per liter of heparin. The basic technique and the steps involved in each one of the anastomotic procedures are exposed in Figure 1. Hemodynamic measurements included determination of blood pressure of the donor's aorta and pulmonary artery, recipient's aorta blood pressure and determination of cardiac output of the transplanted heart in selected cases. One to two hours after transplantation the heart was examined macroscopically for any gross alterations. Samples from the left ventricle, right ventricle, and atriums were taken for light histology.

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Address reprint requests to: Luis H. Toledo Pereyra, MD, PhD, Department of Surgery, Section of Transplantation and Surgical Research, Mt. Carmel Mercy Hospital, 6071 West Outer Drive, Detroit, Michigan, 48235.

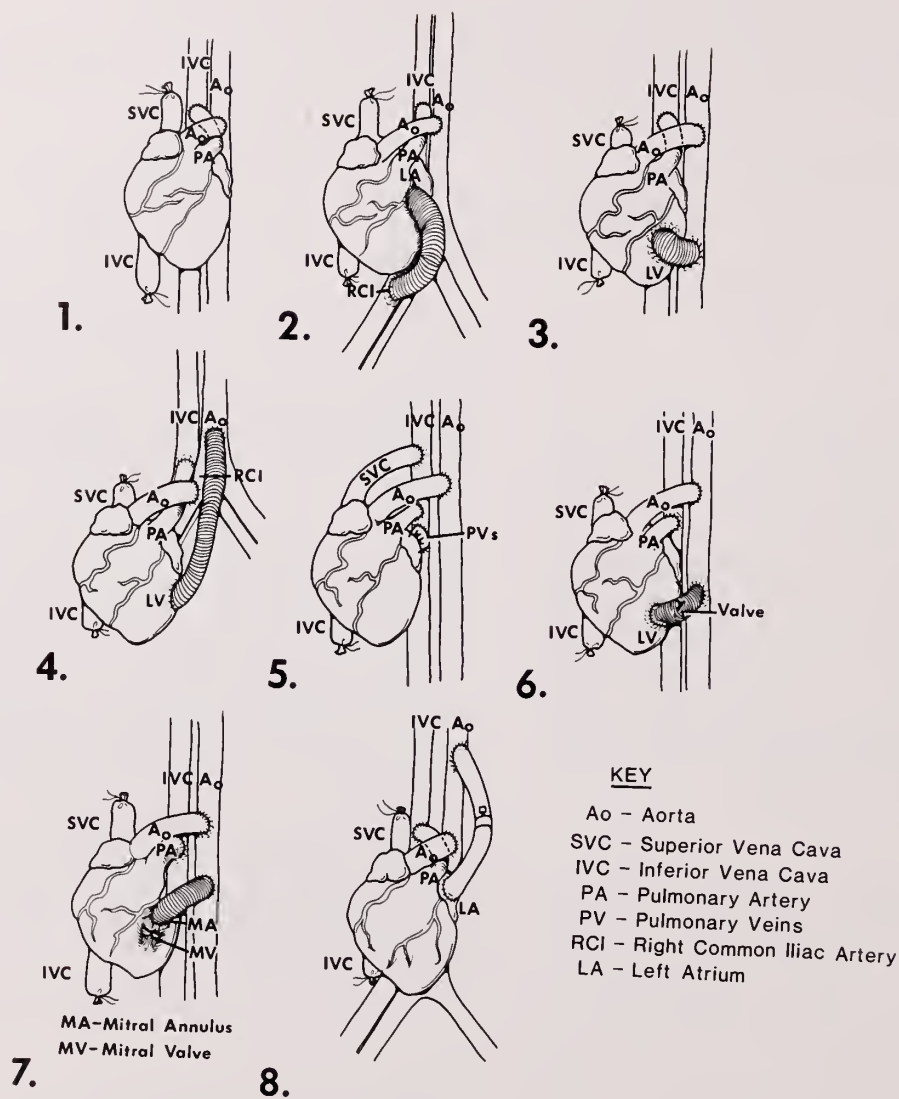


Figure 1: Abdominal heart transplantation models.

Results

The hemodynamic data obtained from these transplants indicate that the first six transplantation models did not support the circulation, the cardiac output of the transplanted hearts was less than 0.9 L/min (Table I). Model No. 7, which consisted of anastomosis of the aorta to aorta, pulmonary artery

to inferior vena cava, and a dacron graft interposition from the mitral annulus to the aorta, showed a cardiac output of 2.0-2.5 L/min, a peak aortic flow of 2.5 L/min and a donor aortic flow of 33 ml/second. Model No. 8 (Figure 2) also showed a good hemodynamic response with support of the circulation even when the recipient's own heart received massive myocardial infarction after the ligation

TABLE I

Hemodynamic Data of the Abdominal Heart Transplantation Models

Heart Transplant Model	Recipient Aorta	Donor Aorta (TX)	LV. Donor Pressure (TX)	PA Pressure (TX)	Cardiac Output (L/min) (TX)
1. Ao-Ao PA-VC	120/80	100/70	80	< 10	0.5
2. Ao-Ao PA-VC RCI-LA	115/75	95/70	75	< 10	0.6
3. Ao-Ao LV-Ao PA-VC	110/70	105/80	95	< 10	0.8
4. Ao-RCI LV-Ao PA-VC	110/75	100/75	90	< 10	0.6
5. Ao-Ao PA-VC VC-VC PV-VC	120/80 300	100/70 300	80	< 10	0.4
6. Ao-Ao LV-Ao (with dacron conduit valved graft) PA-VC	120/80	115/70	90/50	< 10	0.9
7. Ao-Ao Mitral annular to dacron conduit PA-VC	110/75 2.5 l/min peak aortic flow	110/75 33 ml/sec	110/75	< 10	2.0
8. Ao-Ao LA-Ao-graft PA-IVC	120/80	120/75	110/75	< 10	2.1

KEY -

Ao - Aorta

IVC - Inferior Vena Cava

PA - Pulmonary Artery

PV - Pulmonary Veins

RCI - Right Common Iliac Artery

LA - Left Atrium

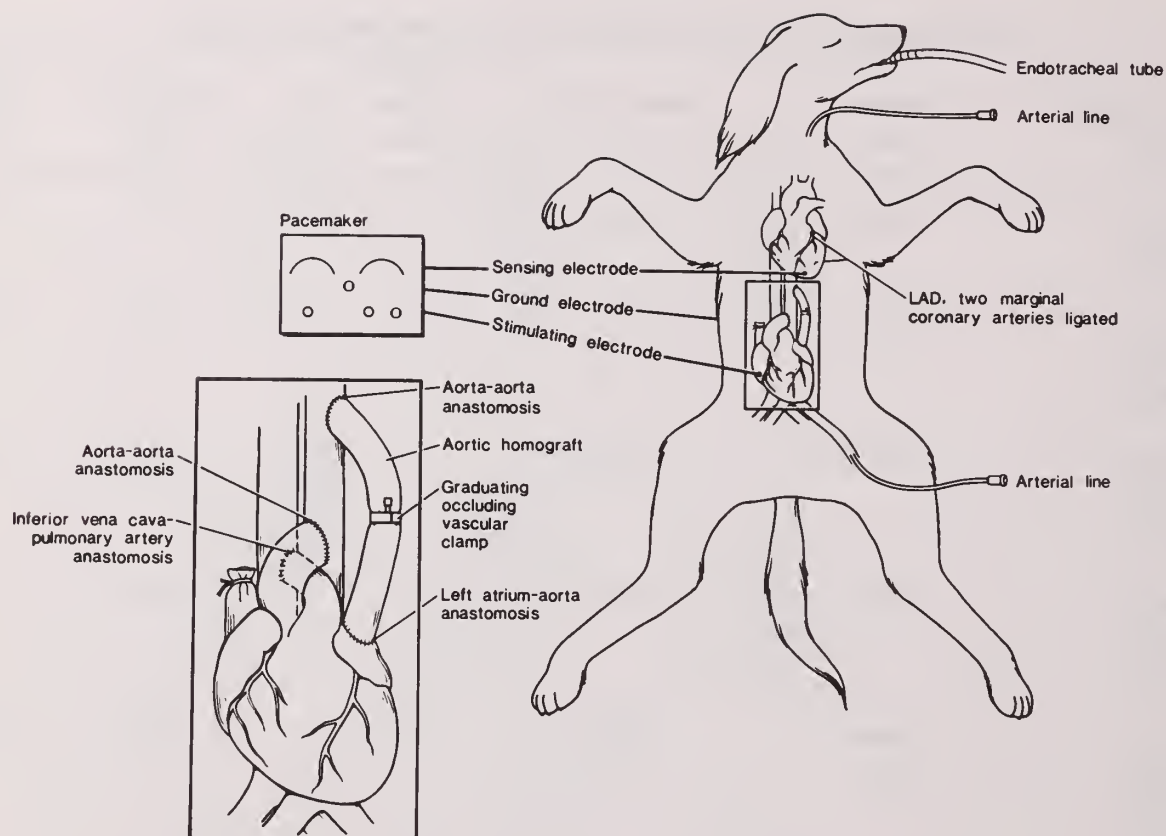


Figure 2: Experimental design of the extrathoracic heart transplantation model No. 8.

of the coronary arteries immediately after transplantation. No significant distention of the atrial chambers was noted, and there was no evidence of ventricular damage. Histologically, models 7 and 8 showed no findings of ventricular edema, muscle disruption or any other significant alterations.

Discussion

Our preliminary studies appear to indicate that it is possible to obtain some circulatory support when the heart transplantation is performed into the abdominal vessels with a direct input into the mitral annulus

or into the left atrium utilizing partial blood flow occlusion from the aorta to the left atrium. Previous models attempting to develop an intra-abdominal heart have failed or have required a significant amount of hemodynamic manipulation that are impractical for clinical application (1). We believe that models 7 and 8 have a definite advantage over previous models utilized for the same purposes (1).

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Children need safety belts too. The arms of a parent or other adult are not strong enough to restrain and protect a small child, even in low speed crashes. If the parent is not wearing a belt, he or she may be thrown forward.

Children up to age 4 should ride in a specially designed infant carrier or child restraint that is secured by the safety belts already in the auto.

Under all circumstances, fasten your safety belts before the ignition is turned on, and keep them fastened whenever the vehicle is in motion. Drivers must demand that passengers buckle up.

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Description: *Tolectin DS* (tolmetin sodium) capsules contain tolmetin sodium as the dihydrate in an amount equivalent to 400 mg of tolmetin. Each capsule contains 36 mg (1.568 mEq) of sodium.

Contraindications: *Tolectin* (tolmetin sodium) should not be used in patients who have previously exhibited intolerance to it or patients in whom aspirin and other non-steroidal anti-inflammatory drugs induce symptoms of asthma, rhinitis or urticaria.

Warnings: Give under close supervision to patients with a history of upper gastrointestinal tract disease and only after consulting the "Adverse Reactions" section. Peptic ulceration and gastrointestinal bleeding, sometimes severe, have been reported.

If *Tolectin* must be given to patients with active peptic ulcer, closely supervise the patients for signs of ulcer perforation or severe gastrointestinal bleeding.

Precautions: *General*—Clinical studies of up to two years duration have shown no changes in the eyes attributable to *Tolectin* (tolmetin sodium) administration; however, because of ocular changes observed clinically with other non-steroidal anti-inflammatory drugs, ophthalmologic examinations should be carried out within a reasonable time after starting chronic therapy and at periodic intervals thereafter.

There has been no evidence of renal toxicity to date in clinical studies; however, since *Tolectin* is eliminated primarily by the kidneys, closely monitor patients with impaired renal function, they may require lower doses.

Tolectin prolongs bleeding time. Patients who may be adversely affected by prolongation of bleeding time should be carefully observed when *Tolectin* is administered.

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Tolectin should be used with caution in patients with compromised cardiac function.

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Usage in Pregnancy—Since *Tolectin* has not been studied in pregnant women, the use of *Tolectin* during pregnancy is not recommended.

Nursing Mothers—Because *Tolectin* may be secreted in human milk, as a general rule nursing should not be undertaken while a patient is on this drug.

Drug Interactions—Although *Tolectin* has been found *in vitro* to bind extensively to plasma protein, it does not alter the dosage of warfarin required to maintain a uniform prothrombin time.

In adult diabetic patients under treatment with either sulfonylureas or insulin, there is no change in the clinical effects of either *Tolectin* or the hypoglycemic agents.

Adverse Reactions: Gastrointestinal System—The most frequent adverse reactions which occurred were gastrointestinal: nausea, 1 in 9 patients, dyspepsia, 1 in 10 patients, abdominal pain, 1 in 15; gastrointestinal distress, 1 in 15; flatulence, 1 in 25; diarrhea, 1 in 25; constipation, 1 in 40; vomiting, 1 in 30; gastritis, 1 in 55; and significant gastrointestinal bleeding without evidence of peptic ulceration, 1 in 240.

The incidence of peptic ulcer in about 3000 patients treated up to two years in clinical studies was about 1 in 50. Thirty-four percent of the ulcer patients had prior history of peptic ulcer disease and/or were receiving concomitant anti-inflammatory drugs, including corticosteroids, known to produce peptic ulceration.

In clinical trials about 10% of patients dropped out because of adverse reactions, mostly gastrointestinal in nature.

Body as a Whole—headache, about 1 in 10 patients; asthenia and chest pain, less frequently; and, rarely, anaphylactoid reactions.

Cardiovascular—edema, about 1 in 15 patients; hypertension, less frequently.

Central Nervous System/Psychiatric—dizziness or lightheadedness, about 1 in 20 patients; tension or nervousness, 1 in 50 patients; drowsiness, 1 in 60 patients; insomnia and depression, less frequently.

Dermatologic—rash, about 1 in 40 patients; pruritus, 1 in 60 patients; skin irritation, 1 in 55 patients.

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ASAMBLEA ANUAL

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ASSOCIATION OF GASTRIC CANCER AND NEPHROTIC SYNDROME - AN IMMUNOLOGIC STUDY IN THREE PATIENTS

Wakashin M, Wakashin Y, Iesato K, et al - Gastroenterology 78 (4): 749-756, 1980.

El síndrome nefrótico se ha reportado como una de las complicaciones de pacientes con tumores. Este síndrome se ha reconocido en pacientes con linfoma, y cáncer de mama, bronquios, y colon. Los autores de este artículo reportan tres pacientes que presentaron clínicamente con un síndrome nefrótico y que posteriormente se les diagnosticó adenocarcinoma gástrico. Biopsias renales demostraron una nefropatía membranosa con depósitos granulares subepiteliales. Material antigénico similar o idéntico a CEA (antígeno carcinoembrionario) se demostró en depósitos inmunes en los glomerulos. Un eluido glomerular marcado con fluorocina reaccionó con células superficiales del tumor gástrico. En un paciente el síndrome nefrótico desapareció después de remover el tumor. Los autores concluyen que la nefropatía en estos pacientes se debió posiblemente a un antígeno asociado con el tumor gástrico.

(Sometido por A. Olazábal, MD)

HYONATREMIA IN PATIENTS WITH SUBARACHNOID HEMORRHAGE. A STUDY OF VASOPRESSIN WITH BLOOD VOLUME

Paul B. Nelson et al - University of Pittsburgh - Paper presented at the American Association of Neurological Surgeons, New York City April 20, 1980.

Hyponatremia and renal sodium loss is especially important in patients with subarachnoid hemorrhage since the clinical picture may resemble vasospasm. The patient becomes progressively more lethargic and deteriorates.

In a study of 17 patients with subarachnoid hemorrhage all had elevated ADH and 14 had hyponatremia attributed to inappropriate ADH secretion. The surprising finding was a decreased blood volume in the patients with inappropriate ADH since with a contracted blood volume there should be no stimulus for excessive ADH production.

The importance of this finding is that where hyponatremia is ordinarily treated by fluid restriction, in this instance, the contracted blood volume is treated with colloid replacement and plasmate or albumin while restricting water intake.

(Submitted by Nathan Rifkinson, MD, VAH)

THE INITIAL CHEST X-RAY IN ACUTE MYOCARDIAL INFARCTION

Battler A, Karliner JS, Higgins CB et al - Circulation 1980:61, 1004-1009.

En este estudio hecho en la Universidad de San Diego, California, los autores comparan los hallazgos en radiografía de pecho de 273 pacientes con infarto agudo y los correlacionan con supervivencia a 3 meses y un año. Las radiografías fueron clasificadas de acuerdo con la severidad de la congestión pulmonar de 0- a 4 (0=ninguna; 1=redistribución apical; 2=edema intersticial; 3=edema alveolar localizada; 4=edema alveolar difusa) y se tomó en cuenta también la presencia

de cardiomegalia. Los resultados fueron los siguientes:

Por Ciento Supervivencia 3 meses

94	80	69	60	18
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Por Ciento Supervivencia 1 año

88	65	41	50	0
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La presencia de cardiomegalia alteró estas cifras mínimamente. Los autores llegan a la conclusión que la radiografía de pecho en las primeras 24 horas de infarto agudo es de gran utilidad en identificar los pacientes con buen pronóstico (mortalidad baja) y separarlos de los pacientes con mal pronóstico (mortalidad alta).

(Sometido por Guillermo Cintrón, MD)

DIAGNOSTICO DE LABORATORIO DE LA ENFERMEDAD DEL LEGIONARIO

American Review on Respiratory Diseases - Vol. 121 - 1980
Page 317

La enfermedad del Legionario es una enfermedad sistémica bacteriana con manifestación principal en el pulmón causada por un bacilo gram negativo *Legionella Pneumophila*.

Los autores aprovechando la aparición de un brote de la enfermedad en el Hospital de Veteranos de Wadsford evalúan la utilidad de los métodos de laboratorios para confirmar el diagnóstico de la condición.

A todos los pacientes sospechosos de tener la enfermedad se le tomaron muestras de suero y de secreciones del tracto respiratorio. También se procesaron líquido pleural, tejido pulmonar y cultivos de sangre. Se estableció para procesar todas las muestras un laboratorio especial.

Métodos de Diagnóstico

A- *Inmunofluorescencia Indirecta* (IFA) del suero para medir las concentraciones del anticuerpo usando organismos muertos por el calor. Este método tiene cuatro serogrupos dependiente del antígeno usado. 1- Philadelphia, 2- Togus, 3- Bloomington y los Angeles. El diagnóstico fue positivo si había un aumento de por lo menos cuatro veces el original y mayor a una concentración a 1:128.

B- *Inmunofluorescencia Directa* de las muestras (DFA). Aquí la presencia de 5 o más organismos fluorescentes en cualquier espécimen fue considerado como positivo.

C- *Estudios Bacteriológicos*. Se usan medios artificiales para los organismos seróbicos y anaeróbicos y se usó el medio de carbón y levadura para *Legionella Pneumophila*. Todos los cultivos positivos se enviaron al CDC para su confirmación.

D- Ensayo de método Inmunosorbentes de enzimas en especímenes de orina para la presencia de *Legionella Pneumophila* usando el serogrupo 1 antígeno.

Treinta y dos veces la Enfermedad del Legionario fue diagnosticada en pacientes con pulmonía adquirida de origen nosocomial usando Inmunofluorescencia directa (DFA) Inmunofluorescencia Indirecta (IFA) y el cultivo de *Legionella Pneumophila* del tracto respiratorio.

Los cultivos fueron positivos en 13 de 21 pacientes con muestras apropiadas. Al usar el cultivo positivo como definición de la enfermedad la sensibilidad del método de Inmunofluorescencia directa fue de 62 por ciento y el de Inmunofluorescencia indirecta en el suero 75 por ciento.

Al usarse un grupo de 21 pacientes sin la Enfermedad del Legionario como grupo control se notó que la especificidad del método de Inmunofluorescencia directa fue de 94 por ciento y la especificidad de la inmunofluorescencia indirecta fue de 75 por ciento.

El cultivo de las muestras fue necesario para diagnosticar algunos casos de la enfermedad al

fallar las otras dos pruebas de laboratorio. Los autores recomiendan el uso de los tres métodos de diagnóstico para aumentar la sensibilidad y especificidad del diagnóstico.

(Sometido por Ramón E. Figueroa Lebrón, MD)

REHABILITATION PRINCIPLES IN THE CARE OF GYNECOLOGIC AND OBSTETRIC PATIENTS

Maly BJ, *Arch Phys Med Rehabil.* 61: 78-81, 1980.

Literatura relacionada con discapacidad y rehabilitación en pacientes obstétricos y ginecológicos está muy limitada. Entre los problemas musculoesqueléticos, vasculares, neurológicos, hormonales y sexuales descritos, laxitud del suelo pélvico es la etiología de varios estados disfuncionales y es común tanto en mujeres *paras* como en *no-paras*. El foco de este artículo está dirigido a uno de los estados disfuncionales-incontinencia urinaria-que en trabajos previos tenía una incidencia de 30 por ciento de todas las mujeres y podría afectar hasta un 63 por ciento de las mujeres menopáusicas. Este estudio, aplicando principios de rehabilitación a diagnóstico y tratamiento, encontró la incidencia de incontinencia urinaria de ser de 20 a 30 por ciento en mujeres, embarazadas o no, que no hicieron ejercicios específicos de suelo pélvico. Un grupo de mujeres, no embarazadas, que hicieron ejercicios Kegel para fortalecimiento de suelo pélvico, solo tuvo una incidencia de incontinencia urinaria de 6 por ciento. Existe una necesidad para determinar si el ejercicio de suelo pélvico, hecho efectivamente, puede minimizar este problema en mujeres postmenopáusicas. Principios de rehabilitación pueden ser aplicados al diagnóstico y tratamiento a otras condiciones incapacitantes en ginecología y obstetricia.

(Sometido por Rafael Alvarez, MD)

THE VALUE OF ORTHOSES FOR PATIENTS WITH DUCHENNE MUSCULAR DYSTROPHY

Zitler, Fred A. and Kent G., *Physical Therapy*, Nov. 1979, 59: 11: 1361-1365.

Estudio prospectivo con 17 pacientes de distrofia muscular tipo Duchenne de seis años de duración. A los pacientes se le suplió una abrazadera tipo "Knee ankle-foot". Luego de un período de tres meses se estudió la efectividad del tratamiento. (Cuántos ambulaban independientemente) Siete (7) pacientes (41 por ciento) pudieron andar 20 pies en un minuto (considerando ambulación apropiada), cuatro (4) pacientes (23 por ciento) pudieron ambular pero a menor velocidad y seis (6) (35 por ciento) pudieron estar de pie sin ambular. Se concluye que (1) las abrazaderas son más efectivas en niños que ambulan independientemente hasta los 10 años, (2) niños que tienen un 50 por ciento de fuerza muscular al tiempo que empieza a usar las abrazaderas y (3) niños que no tienen problemas adicionales de obesidad o retraso mental.

También se presentan otras consideraciones que aunque menores, hay que individualizarlas en cada caso para predecir la efectividad de la abrazadera.

(Sometido por José A. Arabaia, MD)

PAIN SYMPOSIUM

International Rehabilitation Medicine, 1979, 1:3:100-120, EULAR Publishers, P. O. Box 146, CH-4011 Basel, Switzerland.

Simposio sobre el dolor presentado en 4 artículos. El primero presenta la base de las dos teorías prevalecientes sobre la percepción del dolor, estas son: (1) que el estímulo de dolor tiene tractos "privados" hasta áreas específicas centrales, y (2) que

el dolor deriva sus características según las áreas cerebrales que registren los estímulos.

El segundo artículo elabora en la teoría del "gate control." La anatomía, bioquímica y fisiología de la sustancia gelatinosa son expuestas.

El tercer artículo gira alrededor de los resultados con la estimulación eléctrica transcutánea como moduladora del dolor.

El cuarto y último artículo se basa en la experiencia con 103 pacientes de dolor crónico los cuales experimentaron alivio cuando fueron tratados con fármacos psicotrópicos. Las ventajas, modo de acción y dosis de estas drogas es descrita.

(Sometido por José A. Arabia, MD)

GOLD THERAPY IN THE MANAGEMENT OF JUVENILE RHEUMATOID ARTHRITIS

Earl J. Brewer, Jr., Edward H. Giannini, and Elizabeth Barkley, Texas Children's Hospital, Houston, Texas

Gold therapy for 6 months was shown to be efficacious in reducing the severity of articular manifestations in 32 (63 percent) of 51 juvenile rheumatoid arthritis patients reviewed retrospectively. Similarly, reductions in the total number of involved joints were seen in 25 (49 percent) patients. Patients in whom a favorable response to therapy was noted had more severe joint involvement at the start of therapy than did noresponders. In general, patients who responded experienced considerable improvement. Duration of disease prior to gold therapy initiation and disease onset type were not related to the probability of favorable response. Incidence of adverse side effects was low. Gold has recently been approved by the Food and Drug Administration for use in children.

(Sometido por Edwin Mejías, MD)

ENDURANCE TRAINING AND CARDIOVASCULAR FUNCTIONS IN 9 AND 10 YEAR OLD BOYS

Wendel Gatch, PhD, Ronald Byrd, PhD, Arch Phys Med, Rehabil. Vol 60: 574-577, 1979.

Treinta y dos niños de nueve y diez años de edad fueron seleccionados y divididos al azar en un grupo experimental y un grupo control para así poder investigar las respuestas cardiovasculares a intervalos de entrenamiento. Se hicieron cuatro etapas de trabajo de cuatro minutos cada una, separadas por intervalos de 3 minutos de recuperación cada día por 8 semanas. Las cargas de trabajo fueron prescritas de manera tal que las frecuencias cardíacas fluctuaron entre 170-195 para cada etapa de trabajo (80-90 por ciento del máximo estimado). El grupo control tomó parte en períodos de educación física o tradicionales durante el tiempo del estudio. Valores basales antes del entrenamiento fueron determinados por el consumo de oxígeno, frecuencia cardíaca y gasto cardíaco. Las cargas fueron aumentadas progresivamente para determinar la capacidad de trabajo físico a una frecuencia cardíaca de 170. Los exámenes fueron repetidos después de las ocho semanas de entrenamiento con cargas de trabajo idénticas a los valores pre entrenamiento. Análisis de los resultados revelaron que ocurrieron mejoras significativas en el grupo experimental en el "Stroke Volume" y el pulso de oxígeno. Un aumento del 6.5 por ciento en el "Stroke Volume" fue contrarrestado por un 6.8 por ciento de disminución en la frecuencia cardíaca; resultado en ninguna diferencia de gasto cardíaco. Aumentos en las capacidades de trabajo ocurrió en cada grupo pero solo en el grupo experimental fueron significativos. No se detectaron diferencias en los grupos en cuanto al consumo de oxígeno a la diferencia de oxígeno arteriovenoso. Se concluyó que niños a este nivel de edad se adaptaron rápidamente al stress cardiovascular. Se sugirió que si el stress cardiovascular mejorado se considera como una meta válida de los programas de educación física entonces se deben suplementar los programas tradicionales en deportes con procedimientos diseñados específicamente para dar resistencia.

(Sometido por Tomás U. Poventud, MD)

PULMONARY DYSFUNCTION FOLLOWING TRAUMATIC QUADRIPLÉGIA

John C. McMidron, MD, BS, PnD, Lux Midid, MD, Philip R. Westfroos, MD - JAMA Vol. 243 No. 6: 528-531, 1980.

Un estudio prospectivo de las complicaciones pulmonares ocurridos en veintidós pacientes consecutivos que fueron admitidos al hospital dentro de las 24 horas de ocurrido una quadriplegia traumática, fue comparado con los hallazgos retrospectivos de 22 pacientes comparables. Los pacientes en el grupo prospectivo recibieron terapia diseñada a prevenir o revertir la retención de secreciones. Todos los pacientes en este grupo sobrevivieron. En el grupo retrospectivo hubo nueve muertes; complicaciones pulmonares y la necesidad de intubación endotraqueal con ventilación mecánica fueron tres veces más frecuentes.

Estos estudios revelan que la atención de cerca a la prevención, reconocimiento y tratamiento de la retención de secreciones y atelectasias pueden contribuir grandemente a disminuir la mortalidad, la incidencia de complicaciones pulmonares y en la necesidad de dar ventilación de sostén después de ocurrir una quadriplegia traumática. Estudios de función pulmonar en secuencia demostraron un marcado grado de disfunción respiratoria y una mejoría significativa con el pasar del tiempo. Esta mejoría resultó probablemente por fortalecimiento del diafragma combinado con un aumento en estabilidad de la caja torácica y pared abdominal ya que el comienzo de la espasticidad envuelve los músculos intercostales y los abdominales anteriores.

Además de que la atención presente al involucramiento pulmonar con programas vigorosos de terapia han sido factores importantes en los resultados del estudio, también se deben considerar los posibles avances en el tratamiento de lesiones del cordón espinal y los cambios de actitudes ocurrido en el período del estudio, orientados al cuidado del paciente quadriplégico.

(Sometido por Tomás U. Poventud, MD)

AMYLOID NEUROPATHY AND TREMOR IN WALDENSTROM'S MACROGLOBULINEMIA

S. Bajada, F. Mastaglia, MD, A. Fisher, ARchs. Neurol. Vol 37, 240-242, 1980.

Envolvimiento central y periférico del sistema nervioso se puede encontrar en la macroglobulinemia de Waldenstrom's siendo la neuropatía periférica la complicación más frecuente. En el sistema nervioso central incluyen derrames cerebrales debido a lesiones del cerebro focales, hemorragias subaracnoides y síndromes multifocales del cerebro. Desórdenes extrapiramidales son poco comunes.

En este artículo los autores describen un caso de macroglobulinemia de Waldenstrom's con neuropatía causada por depósitos de amiloide y además un síndrome parkinsoniano. Se descubren los hallazgos en una biopsia del nervio sural con el microscopio de luz y el microscopio electrónico y se discuten los posibles mecanismos patogénicos en la producción de la neuropatía.

Esta se puede manifestar como una polineuropatía sensorimotora, predominante sensorial, como una mononeuropatía o mononeuritis múltiple que puede envolver los nervios craneales. La patogénesis de la neuropatía es controversial y se postulan varios mecanismos.

En el presente caso, la neuropatía fue asociada con depósitos de amiloide. Infiltrados celulares en el nervio sural eran bien difusos y no había evidencia de depósitos de inmunoglobulinas en las fibras nerviosas como había sido descrito en casos anteriores.

Este caso constituye el cuarto en el cual se encuentran depósitos de amiloide definitivos y el segundo en el cual la presencia de amiloide es confirmada por el microscopio electrónico.

(Sometido por Tomás U. Poventud, MD)

LAS CONSECUENCIAS PULMONARES DE ASPIRACION DE CONTENIDO GASTRICO A pH MAYOR DE 2.5

Daniel J. Schwartz, James W. Wynne, et al - American Review of Respiratory Disease, 121: 119-126, 1980.

En este estudio utilizando perros, los autores refutan la idea prevaleciente que aspiraciones

gástricas a pHs mayores de 2.5 son benignas. Los resultados de administrar intratraquealmente ácido hidrolórico definitivamente demuestran hipoxemia severa a pH de 1.8 y 5.9. La adición de partículas de comida a ambas soluciones ácidas, ocasionaron reacciones inflamatorias, granulomatosas peribronquiales en los animales estudiados.

(Sometido por Iván León, MD)



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*In vitro data do not necessarily predict clinical efficacy.

1. PMR Bacteriologic Report, Summer Series 1979; a national bacteriologic monitoring service for 200 acute-care hospitals of 100 beds or more.

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The drug is also contraindicated in those patients with known hypersensitivity to Macrochantin, Furadantin® (nitrofurantoin), and other nitrofurantoin preparations.

WARNINGS: Acute, subacute and chronic pulmonary reactions have been observed in patients treated with nitrofurantoin products if these reactions occur, the drug should be withdrawn and appropriate measures should be taken.

An insidious onset of pulmonary reactions (diffuse interstitial pneumonitis or pulmonary fibrosis, or both) in patients on long-term therapy warrants close monitoring of these patients.

There have been isolated reports giving pulmonary reactions as a contributing cause of death. (See Hypersensitivity reactions.) Cases of hemolytic anemia of the primaquine sensitivity type have been induced by Macrochantin. The hemolysis appears to be linked to a glucose-6-phosphate dehydrogenase deficiency in the red blood cells of the affected patients. This deficiency is found in 10 percent of Negroes and a small percentage of ethnic groups of Mediterranean and Near-Eastern origin. Any sign of hemolysis is an indication to discontinue the drug. Hemolysis ceases when the drug is withdrawn.

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Hepatitis, including chronic active hepatitis, has been observed rarely. Fatalities have been reported. The mechanism appears to be of an idiosyncratic hypersensitivity type.

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Usage in Pregnancy: The safety of Macrochantin during pregnancy and lactation has not been established. Use of this drug in women of childbearing potential requires that the anticipated benefit be weighed against the possible risks.

ADVERSE REACTIONS: **Gastrointestinal reactions:** Anorexia, nausea and emesis are the most frequent reactions, abdominal pain and

diarrhea occur less frequently. These dose-related toxicity reactions can be minimized by reduction of dosage, especially in the female patient. Hepatitis occurs rarely.

Hypersensitivity reactions: Pulmonary sensitivity reactions may occur, which can be acute, subacute, or chronic.

Acute reactions are commonly manifested by fever, chills, cough, chest pain, dyspnea, pulmonary infiltration with consolidation or pleural effusion on x-ray, and eosinophilia. The acute reactions usually occur within the first week of treatment and are reversible with cessation of therapy. Resolution may be dramatic.

In subacute reactions, fever and eosinophilia are observed less often. Recovery is somewhat slower, perhaps as long as several months. If the symptoms are not recognized as being drug related and nitrofurantoin is not withdrawn, symptoms may become more severe.

Chronic pulmonary reactions are more likely to occur in patients who have been on continuous nitrofurantoin therapy for six months or longer. The insidious onset of malaise, dyspnea on exertion, cough, and altered pulmonary function are common manifestations. Roentgenographic and histologic findings of diffuse interstitial pneumonitis or fibrosis, or both, are also common manifestations. Fever is rarely prominent.

The severity of these chronic pulmonary reactions and the degree of their resolution appear to be related to the duration of therapy after the first clinical signs appear. Pulmonary function may be permanently impaired even after cessation of nitrofurantoin therapy. This risk is greater when pulmonary reactions are not recognized early.

Dermatologic reactions: Maculopapular, erythematous, or eczematous eruption, pruritus, urticaria, and angioedema.

Other hypersensitivity reactions: Anaphylaxis, asthmatic attack in patients with history of asthma, cholestatic jaundice, hepatitis, including chronic active hepatitis, drug fever, and arthralgia.

Hematologic reactions: Hemolytic anemia, granulocytopenia, leukopenia, eosinophilia, and megaloblastic anemia. Return of the blood picture to normal has followed cessation of therapy.

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References: 1. Wallenstein SL, Houde RW: *Fed Proc* 13:414, 1954. 2. Batterman RC, Grossman AJ: *Fed Proc* 14:316, 1955. 3. Vickers FN: *Gastrointest Endosc* 14:94, 1967. 4. Fein FT: *Ann Allergy* 29:598, 1971. 5. Mielke CH, et al: *JAMA* 235:613, 1976. 6. Vernon WG: *Curr Ther Res* 14:801, 1972. 7. Miller AR: *Curr Ther Res* 19:444, 1976. 8. Walker JM: *Curr Ther Res* 15:249, 1973.

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**Because there's nothing mild
about mild hypertension**

BRIEF SUMMARY

Indications: Hypertension, adjunctive therapy in edema. **Contraindications:** Anuria, hypersensitivity to chlorthalidone or other sulfonamide-derived drugs. **Warnings:** Should be used with caution in severe renal disease, impaired hepatic function or progressive liver disease. May add to or potentiate the action of other antihypertensive drugs. Sensitivity reactions may occur in patients with a history of allergy or bronchial asthma. There is a possibility of exacerbation or activation of systemic lupus erythematosus with thiazides, which are related to chlorthalidone. This has not been reported with chlorthalidone. Thiazides cross the placental barrier and appear in cord blood. Use in pregnant women requires that the anticipated benefits of the drug be weighed against possible hazards to the fetus. These hazards include fetal or neonatal jaundice, thrombocytopenia, and possibly other adverse reactions which have occurred in the adult. In nursing mothers, thiazides cross the placental barrier and appear in breast milk. If use of the drug is essential, the patient should stop nursing. **Precautions:** Periodic determination of serum electrolytes to detect possible electrolyte imbalance should be performed at appropriate intervals. All patients receiving chlorthalidone should be observed for clinical signs of fluid or electrolyte imbalance, namely, hyponatremia, hypochloremic alkalosis, and hypokalemia. Serum and urine electrolyte determinations are particularly important when the patient is vomiting excessively or receiving parenteral fluids. Medication such as digitalis may also influence serum electrolytes. Hypokalemia may develop with chlorthalidone as with any other potent diuretic, especially with brisk diuresis, when severe cirrhosis is present, or during concomitant use of corticosteroids or ACTH. Interference with adequate oral electrolyte intake will also contribute to hypokalemia. Digitalis therapy may exaggerate metabolic effects of hypokalemia especially with reference to myocardial activity. Any chloride deficit is generally mild and usually does not require specific treatment except under extraordinary circumstances (as in liver disease or renal disease). Dilutional hyponatremia may occur in edematous patients in hot weather. Hyperuricemia may occur or gout be precipitated in certain patients. Insulin requirements in diabetic patients may be increased, decreased, or unchanged and latent diabetes mellitus may become manifest. Chlorthalidone and related drugs may increase the responsiveness to tubocurarine. The antihypertensive effects of the drug may be enhanced in the postsympathectomy patient. Chlorthalidone and

related drugs may decrease arterial responsiveness to norepinephrine. If progressive renal impairment becomes evident, as indicated by a rising nonprotein nitrogen or blood urea nitrogen, a careful reappraisal of therapy is necessary with consideration given to withholding or discontinuing diuretic therapy. Chlorthalidone and related drugs may decrease serum PBI levels without signs of thyroid disturbance. **Adverse Reactions:** Anorexia, gastric irritation, nausea, vomiting, cramping, diarrhea, constipation, jaundice (intrahepatic cholestatic jaundice), pancreatitis, dizziness, vertigo, paresthesias, headache, xanthopsia, leukopenia, agranulocytosis, thrombocytopenia, aplastic anemia, purpura, photosensitivity, rash, urticaria, necrotizing angitis (vasculitis) (cutaneous vasculitis), Lyell's syndrome (toxic epidermal necrolysis). Orthostatic hypotension may occur and may be aggravated by alcohol, barbiturates or narcotics. Other adverse reactions include hyperglycemia, glycosuria, hyperuricemia, muscle spasm, weakness, restlessness, impotence. Whenever adverse reactions are moderate or severe, chlorthalidone dosage should be reduced or therapy withdrawn. **Usual Dose:** One tablet daily. **How Supplied:** Tablets—100 mg. (white, scored), 50 mg. (aqua) in bottles of 100, 1000 and 5000; 25 mg. (peach) in bottles of 100 and 1000; unit-dose blister packs, boxes of 100 (10 x 10 strips).

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1. Five-year Findings of the Hypertension Detection and Follow-up Program: 1. Reduction in Mortality of Persons With High Blood Pressure, Including Mild Hypertension, JAMA 242: 2562, Dec. 7, 1979. 2. Payne, G. H. Presentation of HDFP findings (Nov. 27, 1979), data on file, USV Laboratories.

USV
LABORATORIES

USV Laboratories Inc.
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M E D I - Q U I Z

LOWN GANONG LEVINE SYNDROME

1. Paciente varón de 58 años, diabético en 57 unidades de insulina se presenta en la clínica de endocrinología para evaluación de rutina. Electrocardiograma al reposo demostró intervalo PR de .10 segundos. El complejo QRS era normal. ¿Qué otro estudio no-invasivo recomendaría en este momento?
 - a) Vectocardiograma
 - b) Ecocardiograma
 - c) Registro del Haz de His
 - d) Electrocardiografía dinámica
 - e) Ninguna
2. El paciente fue referido al cardiólogo para evaluación de palpitaciones recurrentes. Estos episodios ocurrían de forma espontánea. En ocasiones tenían un comienzo rápido y terminaban abruptamente. El consultor recomendó:
 - a) Empezar terapia farmacológica con digital y quinidina
 - b) Estudios electrofisiológicos
 - c) Observación clínica
 - d) Electrocardiografía dinámica por 24 horas (Holter)
3. En pacientes adultos con PR corto ($< .12$ seg) y QRS normal ($< .10$ seg), cuál es el mecanismo responsable por el acortamiento del intervalo PR? Puede haber más de una contestación.
 - a) Nodo A-V pequeño
 - b) Conducción rápida a través del nodo A-V.
 - c) Tracto atrio-nodal o atrio-His
 - d) Tracto atrio-ventricular
 - e) Ninguna
4. El síndrome de Lown-Ganong-Levine (LGL) incluye:
 - a) pacientes con PR cortos y complejo QRS normal
 - b) pacientes con taquicardias supraventriculares recurrentes, intervalos PR cortos y complejo QRS normal.
 - c) a) y b)
 - d) Ninguno
5. El hallazgo electrofisiológico más frecuente en pacientes con PR corto y QRS normal es:
 - a) Intervalos A-H normal
 - b) Intervalos A-H cortos con prolongación mínima de éste durante estimulación atrial en incrementos.
 - c) Intervalos A-H normal y H-V corto
 - d) Curvas duales de conducción atrio-ventricular.
6. Pacientes con el síndrome de LGL pueden presentar: (puede haber más de una alternativa)
 - a) Taquicardia supraventricular paroxística recurrente
 - b) Aleteo atrial con conducción 1:1 respuesta ventricular mayor de 250/minuto
 - c) Fibrilación atrial con respuesta ventricular rápida (mayor de 240/minuto)
 - d) Fibrilación ventricular

(Contestaciones en página 304)

IMMUNOPATHOGENIC MECHANISMS OF LUPUS NEPHRITIS

The basic etiology responsible for the aberrant immunologic reaction in SLE remains unknown; however, the pathogenic mechanisms, particularly that of the renal manifestations, have been clearly established.

Immunofluorescence and electron microscopy studies in experimental and kidney biopsy material have provided ample convincing evidence that lupus nephritis, as most glomerulonephritis, has an immunological pathogenic mechanism. The finding of characteristic ultrastructural and immunofluorescent patterns indicates that lupus nephritis, as many other forms of glomerulonephritis, is an immune complex disease. It differentiates from the other group of immune mediated glomerulonephritis such as the one associated with Good Pasture's syndrome which is due to antiglomerular basement membrane (anti-GBM) antibodies. The finding of *continuous linear* immunofluorescence staining or immuno-electron microscopy localization both for IgG and complement warrants the diagnosis of anti-GBM disease. On the other hand, the demonstration of *granular deposits* containing immunoglobulins and complement as demonstrated by electron and immunofluorescence microscopy in the glomerular tufts warrants the diagnosis of an immune complex glomerulonephritis as is the case of lupus nephritis.

In lupus nephritis, the antigen antibody complexes may be deposited in a variety of patterns each of them typical for a given type or stage of the disease. The injury reaction in SLE involves additional factors besides the deposits of complexes in vessels and glomerular tufts. The inflammatory response is dependent on the activation of the complement cascade system resulting in the formation of vasoactive amines and chemotactic enzymes transforming a pure immunologic

reaction into an inflammatory process.

On the basis of clinical features such as proteinuria, hematuria and/or reduction in glomerular filtration rate, renal involvement occurs in 60-70 percent of patients with SLE. However, the actual incidence of lupus glomerulopathy is much higher. In biopsy studies performed in patients without clinical features of renal disease, abnormal renal histopathology can be demonstrated in the great majority. It is interesting to note that even in the absence of clinical evidence of renal disease, a severe tissue reaction can be present in some cases. This data, therefore, indicates that lupus nephritis is a common finding in SLE and cannot be excluded without a renal biopsy. More recently, it has been demonstrated in several reports that the ultrastructural changes, particularly that related to the localization and degree of accumulation of antigen-antibody complexes correlates very good with the clinical picture and probably provides the most reliable information regarding prognostic and clinical course of the disease.

In this presentation, renal biopsies obtained in 166 patients with SLE including 26 second biopsies are evaluated with the purpose of correlating the light microscopy findings with the immunopathology noted by immunofluorescence and electron microscopy studies in the different types of lupus nephritis. Our experience with lupus nephritis reaffirms recent reported observations which it is suggested that the structural changes in lupus nephritis, particularly those related with the localization and degree of accumulation of antigen antibody complexes as noted by electron microscopy, are of vital importance in the classification, clinical course and prognosis of lupus nephritis. In the se-

cond biopsy, we have noted findings similar to those noted by other investigators in which it can be concluded that what was traditionally known as types of lupus nephritis are different stages of the same disease process.

MEDI-QUIZ

1. The glomerulonephritis of SLE is an AGBM disease. _____
2. The glomerulonephritis of SLE is an immune complex disease. _____
3. The antigen-antibody complexes in SLE are formed in the glomerular capillaries. _____
4. The antibodies in the immune complex deposits of SLE are anti-DNA _____
5. SLE is an autoantibody disease _____
6. The only immunoglobulin found in the immune-complex deposits in lupus nephritis is IgG _____
7. Low serum complement in SLE is frequently associated with active renal disease _____
8. The "micro tubular viral-like" particles found in lupus nephritis are pathognomoni of the disease _____
9. The etiology of SLE have not been discovered _____
10. A focal lupus nephritis never transforms into a diffuse process _____
11. The antinuclear immunofluorescent pattern most frequently found in SLE is peripheral or rim _____

12. The L. E. test is persistently positive in SLE _____

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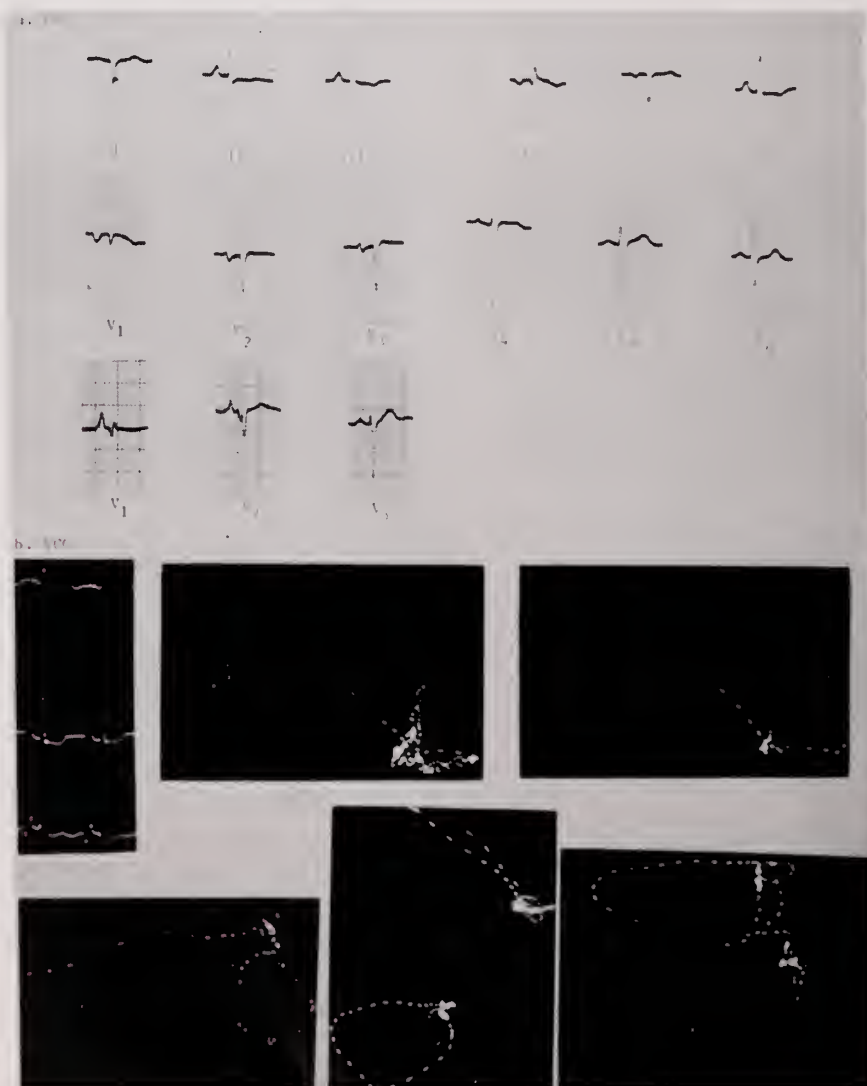
Jesús M. Vázquez, MD
Departamento de Patología
Hospital de Veteranos SJ PR

ELECTROCARDIOGRAM OF THE MONTH

The electrocardiogram (ECG) and Frank vectorcardiogram (VCG), Figure 1, are those of a 48-year-old female with dyspnea, congestive heart failure and increased sputum production. At another date atrial tachycardia with block, atrioventricular dissociation and ventricular bigeminy were present, probably secondary to digitalis intoxication.

DIAGNOSIS

1. Study the traces and describe.
2. What diagnoses are possible from the ECG and VCG?
3. What is your clinical diagnosis?
4. What is the pathogenesis of these findings?





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Like any antihypertensive, use with caution in severe coronary insufficiency, recent myocardial infarction, cerebrovascular disease or chronic renal failure.

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No Single Advantage Determines Drug Choice.

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*Central alpha-adrenergic stimulation decreases sympathetic outflow from the brain, as shown in animal studies.

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Please see last page for brief summary, including warnings, precautions, and adverse reactions.

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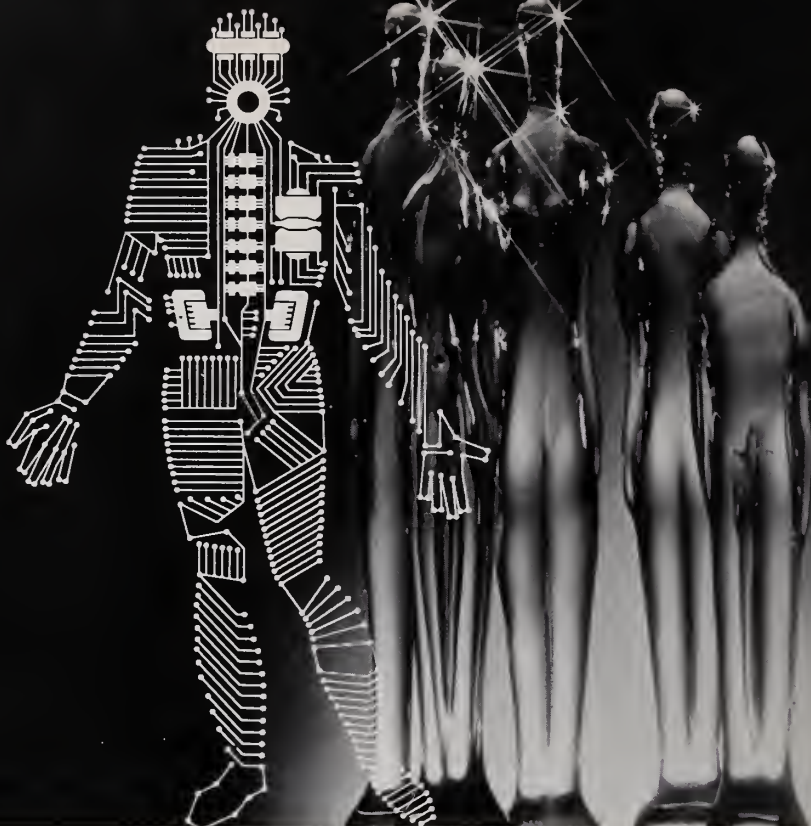
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Indication: The drug is indicated in the treatment of hypertension. As an anti-hypertensive drug, Catapres (clonidine hydrochloride) is mild to moderate in potency. It may be employed in a general treatment program with a diuretic and/or other antihypertensive agents as needed for proper patient response.

Warnings: Tolerance may develop in some patients necessitating a reevaluation of therapy.

Usage in Pregnancy: In view of embryotoxic findings in animals, and since information on possible adverse effects in pregnant women is limited to uncontrolled clinical data, the drug is not recommended in women who are or may become pregnant unless the potential benefits outweigh the potential risk to mother and fetus.

Usage in Children: No clinical experience is available with the use of Catapres (clonidine hydrochloride) in children.

Precautions: When discontinuing Catapres (clonidine hydrochloride), reduce the dose gradually over 2 to 4 days to avoid a possible rapid rise in blood pressure and associated subjective symptoms such as nervousness, agitation, and headache. Patients should be instructed not to discontinue therapy without consulting their physician. Rare instances of hypertensive encephalopathy and death have been recorded after cessation of clonidine hydrochloride therapy. A causal relationship has not been established in these cases. It has been demonstrated that an excessive rise in blood pressure, should it occur, can be reversed by resumption of clonidine hydrochloride therapy or by intravenous phentolamine. Patients who engage in potentially hazardous activities, such as operating machinery or driving, should be advised of the sedative effect. This drug may enhance the CNS-depressive effects of alcohol, barbiturates and other sedatives. Like any other agent lowering blood pressure, clonidine hydrochloride should be used with caution in patients with severe coronary insufficiency, recent myocardial infarction, cerebrovascular disease or chronic renal failure.

As an integral part of their overall long-term care, patients treated with Catapres (clonidine hydrochloride) should receive periodic eye examinations. While, except for some dryness of the eyes, no drug-related abnormal ophthalmologic findings have been recorded with Catapres (clonidine hydrochloride), in several studies the drug produced a dose-dependent increase in the incidence and severity of

The usual starting dose of Catapres is 0.1 mg at breakfast and 0.1 mg at bedtime. Some patients may benefit from a starting dose of 0.1 mg at bedtime.

Usual daily dose range—0.2—0.8 mg

Maximum daily dose—2.4 mg
Doses as high as this have rarely been employed.

For optimal results, the dose of Catapres must be adjusted according to the patient's individual blood pressure response.

spontaneously occurring retinal degeneration in albino rats treated for 6 months or longer.

Adverse Reactions: The most common reactions are dry mouth, drowsiness and sedation. Constipation, dizziness, headache, and fatigue have been reported. Generally these effects tend to diminish with continued therapy. The following reactions have been associated with the drug, some of them rarely. (In some instances an exact causal relationship has not been established.) These include: Anorexia, malaise, nausea, vomiting, parotid pain, mild transient abnormalities in liver function tests; one report of possible drug-induced hepatitis without icterus and hyperbilirubinemia in a patient receiving clonidine hydrochloride, chloralhydrate and papaverine hydrochloride. Weight gain, transient elevation of blood glucose, or serum creatine phosphokinase: congestive heart failure, Raynaud's phenomenon; vivid dreams or nightmares, insomnia, other behavioral changes, nervousness, restlessness, anxiety and mental depression. Also rash, angioneurotic edema, hives, urticaria, thinning of the hair, pruritus not associated with a rash, impotence, urinary retention, increased sensitivity to alcohol, dryness, itching or burning of the eyes, dryness of the nasal mucosa, pallor, gynecomastia, weakly positive Coombs' test, asymptomatic electrocardiographic abnormalities manifested as Wenckebach period or ventricular trigeminy.

Overdosage: Profound hypotension, weakness, somnolence, diminished or absent reflexes and vomiting followed the accidental ingestion of Catapres (clonidine hydrochloride) by several children from 19 months to 5 years of age. Gastric lavage and administration of an analeptic and vasopressor led to complete recovery within 24 hours. Tolazoline in intravenous doses of 10 mg at 30-minute intervals usually abolishes all effects of Catapres, (clonidine hydrochloride) overdosage.

How Supplied: Catapres, brand of clonidine hydrochloride, is available as 0.1 mg (tan) and 0.2 mg (orange) oval, single-scored tablets in bottles of 100 and 1000. Also available as 0.3 mg (peach) oval, single-scored tablets in bottles of 100.

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ANSWER

Pseudoanterior septal myocardial infarction secondary to chronic obstructive pulmonary disease (COPD) and cor pulmonale.

The P wave axis is plus 80-85 degrees and the QRS axis approximately plus 140 degrees. The P waves are peaked in leads I, II, aVF and V₂. There is a striking difference in the configurations of the P's in V₁ above (leads taken 5 months apart) in that they are broad and negative, and in the lower strip in that they are peaked and upright- P pulmonale. QS or only tiny r waves are visible in leads I, aVL, V₁₋₃; a qR complex occurs in aVR and a R/S in V₆. The VCG shows a peaked P wave in lead Y and diphasic P in Z, deep S waves in X and a R (QS) complex in lead Z. The P loops are slightly prominent and oriented inferiorly, both anteriorly and posteriorly. T loops are leftward. The QRS loops are somewhat small and are located mainly rightward, posteriorly and inferiorly. The initial vector is oriented leftward and inferiorly but only slightly anteriorly (decreased anterior forces). The right sagittal and frontal loops rotate clockwise while the horizontal loop is predominantly counterclockwise. Right axis deviation (RAD), right atrial enlargement (perhaps left atrial enlargement also), Type C₁ right ventricular hypertrophy (RVH) and decreased early anterior forces may be diagnosed. These are compatible with COPD and pseudoanterior septal myocardial infarction secondary to cor pulmonale.

Autopsy demonstrated chronic cor pulmonale, chronic bronchitis, emphysema, bronchiectasis, pulmonary and pleural fibrosis and tracheobronchomegaly (Mounier-Kuntz). There was no myocardial infarction or atherosclerotic plaques and the coronary arteries were patent. The measurements were: right and left atria 1 mm, right ventricle 8 mm, left ventricle 15 mm; the heart weight was 380 g.

The classical ECG and VCG may be explained by cardiac and rotational alterations, alterations in the magnitude and direction of the effective axes of the leads, and the posterior terminal QRS forces from activation of the hypertrophied basal region of the right ventricle (Type C RVH). Pseudo-myocardial infarction patterns have been attributed to the relatively superior location of the conventional precordial electrodes in respect to the lowered vertical heart secondary to the low flattened diaphragm and hyperinflated lungs, cardiac septal rotation, right to left septal depolarization, atrialization of the ventricular complex, hypertrophy and dilatation of the right heart, etc.

Sic P pulmonale, S₁S₁₁S₁₁₁ syndrome, Axis Illusion phenomenon, small QRS complexes, large S waves in V₅₋₆ (R/S ratio < 1), fall-off in voltage laterally, "Half Past Six" syndrome, the "Lead 1" sign, vertical or RAD of the P, QRS (plus 90 degrees) and T waves (or minus 90 degrees of the T which tends to be low to inverted throughout) and the other typical signs of COPD favor it over myocardial infarction.

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C U R S O S

CUBAN SOCIETY OF SURGERY - SEGUNDO CONGRESO ANUAL - 26 al 29 de marzo, 1981 - Hotel Caribe Hilton, San Juan, Puerto Rico.

Este programa es patrocinado por la Sección de Cirugía de la Asociación Médica de Puerto Rico. Para más información, favor de comunicarse con el Dr. Esteban Fernández Noda, Edif. Monte Mall Suites 28 y 29, Hato Rey, Puerto Rico 00918.

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January 14-18, 1981 - **ANNUAL NEUROLOGICAL UPDATE**. Eden Roc Hotel, 4525 Collins Avenue, Miami Beach, FL 33140. Sponsor: Department of Neurology, University of Miami School of Medicine. Course Directors: Peritz Scheinberg, MD; D. Ram

Ayyar, MD. CONTACT: Division of Continuing Medical Education D23-3, University of Miami School of Medicine, P. O. Box 016960, Miami, FL 33101. Tel. (305) 547-6716.

March 2-6, 1981. **BASIC NEUROLOGY FOR PSYCHIATRISTS AND GENERALISTS**. Konover Hotel, 5445 Collins Avenue, Miami Beach, FL 33140. Sponsor: Department of Neurology, University of Miami School of Medicine. Course Directors: Robert Davidoff, MD; Robert Shebert, MD. CONTACT: Division of Continuing Medical Education D23-3, University of Miami School of Medicine, P. O. Box 016960, Miami, FL 33101. Tel. (305) 547-6716.

March 23-25, 1981. **PAN-AMERICAN SYMPOSIUM ON TRAUMA OF THE HEAD AND NECK**, Eden Roc Hotel, Miami Beach, FL. Sponsor: University of Miami School of Medicine, Dept. of Otolaryngology. Approved for AMA Category I credit. CONTACT: Division of Continuing Medical Education D23-3, P. O. Box 016960, Miami, FL 33101/call (305) 547-6716. (PRESENTED IN ENGLISH AND SPANISH)

March 26-28, 1981 - **CURRENT CLINICAL CONCEPTS IN OTOLARYNGOLOGY 1981** - Eden Roc Hotel, Miami Beach, FL. Sponsor: University of Miami School of Medicine, Dept. of Otolaryngology. Approved for AMA Category I credit. CONTACT: Division of Continuing Medical Education D23-3, P. O. Box 016960, Miami, FL 33101/call (305) 547-6716. (PRESENTED IN ENGLISH AND SPANISH).

AMA NEWS:

AMA JOURNAL AIRS ISSUE OF HOME VS. HOSPITAL BIRTHS

CHICAGO — So you're going to have a baby! Where?

At home, in a birthing center, or in the hospital?

The issue of home versus hospital birth is becoming increasingly important as consumers, licensing bodies, the government, and other health professionals become more involved in controversies surrounding birth, says G. David Adamson, MD, an obstetrician with Stanford University Medical Center in California.

Writing in the May 2 Journal of the American Medical Association, Dr. Adamson points out that advocates of home birth cite psychological and medical benefits in their demand for a different approach to birthing procedures. While opponents emphasize the risks of home birth and point to improved outcomes through medical progress available only in hospitals.

True facts are skimpy, he says, and do not conclusively support either opinion.

Physicians generally have been antagonistic to home births, preferring the life-saving equipment and surroundings of the modern hospital to enhance safe delivery.

But, says Dr. Adamson, some individuals are going to insist on home birth regardless of safety, and "it is essential that the medical profession become actively involved in an objective analysis of the merits and deficiencies of home and hospital birth settings."

Advocates of home birth believe that the method confers psychological advantages on the parents, the newborn infant, and its brothers and sisters. Some favor home birth because of unpleasant experiences with earlier births in a hospital. They had little choice in birthing methods or activities during labor; could not have family present or have sufficient access to

their baby following birth. They believe hospitals and physicians are authoritarian and impersonal. They want to avoid routine hospital procedures such as cesarean delivery for breech presentation and episiotomy. A major deterrent to hospital birth is the high cost.

The primary opposition to home birth is by physicians who have managed complicated pregnancies. Numerous complications can be foreseen prior to birth and appropriate management planned. But there also are unpredictable complications, such as severe hemorrhage, that could prove fatal outside the hospital. The risks to the fetus are even greater in home births, they say. All births are, to some extent, high risk.

Many physicians and hospitals are providing birth environments that are supportive of the psychological needs of parents and infants, yet women have found it difficult to obtain medical care for out-of-hospital births. One problem is inadequately trained midwives, he says.

Only some 1 percent of American births occur at home and an additional unknown percentage in birthing centers. The big majority of infants are born in hospitals.

Childbirth is not an illness, yet it is associated with increased risk to health, Dr. Adamson points out. Therefore, despite some differences of opinion, almost all physicians and even many people involved in home birthing believe that women having home births face real risk not present in a hospital.

In childbirth, first priority is a living and healthy mother; second, a live and healthy baby; and, third, a psychologically rewarding experience for the parents and baby, Dr. Adamson says.

SNAKE VENOM FAILS AS TREATMENT FOR AMY-

OTROPHIC LATERAL SCLEROSIS

CHICAGO — Snake venom has been tried and found wanting as a treatment for amyotrophic lateral sclerosis, says a Texas research report in the April issue of an American Medical Association specialty journal, *Archives of Neurology*.

There is no satisfactory treatment for amyotrophic lateral sclerosis (ALS) other than relieving the symptoms. A "partial treatment" with detoxified snake venom has been suggested by some researchers, says Victor M. Rivera, MD, neurologist, of Baylor College of Medicine and the Neurosensory Center of Methodist Hospital, Houston.

Dr. Rivera tested the venom with 64 ALS patients. The transient periods of improvement that are peculiar to this disease were more common in the patients receiving placebo than in those receiving venom therapy, he says, and none of the patients showed any benefit from the treatment.

The venom showed some good results in animal studies, and had been found useful in treating a certain type of herpes simplex eye infection in humans. But it failed in ALS, says Dr. Rivera.

Amyotrophic lateral sclerosis is a chronic progressive disease of the nervous system. It most often hits those in their 50s and 60s, but sometimes can strike younger individuals. There is weakness and wasting of muscles and twitchings of nerves. The patient may have episodes of inappropriate crying or laughing. Hands, arms and feet become progressively useless. Facial muscles waste away. In most cases death occurs within three to four years after onset of symptoms.

MEN ALSO GET BREAST CANCER

CHICAGO — Men occasionally get breast cancer.

And their response to treatment is about the same as that of women.

Some 90 men with breast cancer were referred to the M. D. Anderson Hospital and Tumor Institute in Houston over a period of 30 years. A study of the records of 18 of these men is published in the May 2 *Journal of the American Medical Association*.

The 18 were men with advanced breast cancer who were treated with single drugs, rather than a combination of drugs as is sometimes used. There was an overall response of 44 percent who showed improvement. This is about the same percentage as noted in women with advanced breast cancer treated in the same manner, says Dr. Whee-Yong Yap.

The outlook was not favorable for the men in this study. Median survival for those who showed some response to the drug treatment was 23 months. Median survival for those who failed to respond was 14.5 months.

What the study found is that advanced male breast cancer has the same order of responsiveness to drugs as advanced female breast cancer, and the treatment of men should parallel that used for women, Dr. Yap concludes.

*4TH CONGRESS OF THE INTERNATIONAL REHABILITATION MEDICINE ASSOCIATION**PRESS RELEASE:*

The Fourth World Congress of the International Rehabilitation Medicine Association will meet in San Juan, Puerto Rico, April 18-24, 1982.

The Congress theme is "New Findings That Influence Disease and Rehabilitation", which is also the title of a 36-hour, AMA CME Category I, accredited course, divided into twenty, two-hour seminars during the mornings and two, eight-hour sessions during the afternoon. The speakers will be distinguished investigators in the medical sciences. In addition, there is provision for individual papers and scientific films relating to the congress theme. IRMA is a society of physicians from all the fields of medicine and sur-

gery interested in rehabilitation medicine. At present, there are about 1800 members from 70 countries. President is Dr. Wilhelm M. Zinn, Switzerland and Secretary, Dr. Christopher Evans, United Kingdom. For information address: Dr. Herman J. Flax, Chairman IRMA IV, P. O. Box 11696, Caparra Station, Puerto Rico 00922 USA.

NEWS RELEASE FROM THE MEDICAL ECONOMICS COMPANY - A Division of Litton Industries, Inc., Oradell, N. J. 07649

SPORTS MEDICINE FOR THE ATHLETIC FEMALE, just published by Medical Economics Books, is a definitive manual for the "care and feeding" of women athletes. Edited by Dr. Christine E. Haycock, a woman athlete as well as a surgeon, the book includes the work of 30 authorities in physical education and medical specialties, and is thought to be the first book directed specifically to the female athlete and her medical problems.

Photographs, line drawings, and charts enhance the book's readability and usefulness. So do clearly defined chapter headings such as "History

and physical examination of the school-age female athlete;" "A woman's foot in sports;" "General and special orthopedic problems;" "Cardiovascular considerations;" "Gynecologic and endocrine factors;" "Pregnancy and the athlete;" "Proper clothing and equipment;" "Women at the service academies;" "Psychology of the female athlete;" "Guidelines and controversies in sports."

Female athletes, their coaches and trainers, primary physicians, nurses, emergency room personnel, and anyone with direct athlete/patient contact will want to read this book for its reliable medical advice and for its help in improving athletic performance and preventing sports injuries.

Dr. Haycock is an associate professor of surgery at the New Jersey Medical School in Newark, N. J., as well as a Registered Nurse. She is a regular contributor to medical journals and lay publications, and the author of another book, TOTAL WOMAN'S FITNESS GUIDE. She is also in demand as a speaker at surgery seminars and has appeared on local and national radio and TV to talk about women's sports and orthopedic problems. She has fenced competitively, was New Jersey Fencing Champion in 1949-50, and has been a softball pitcher for 30 years.

SPORTS MEDICINE FOR THE ATHLETIC FEMALE is available from the publisher at \$27.50 per copy, plus a \$1 handling charge. Payment should accompany orders to Medical Economics Books (2120-DPRDO), Box 157, Florence, Ky 41042.

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AVISO NEUROLOGOS

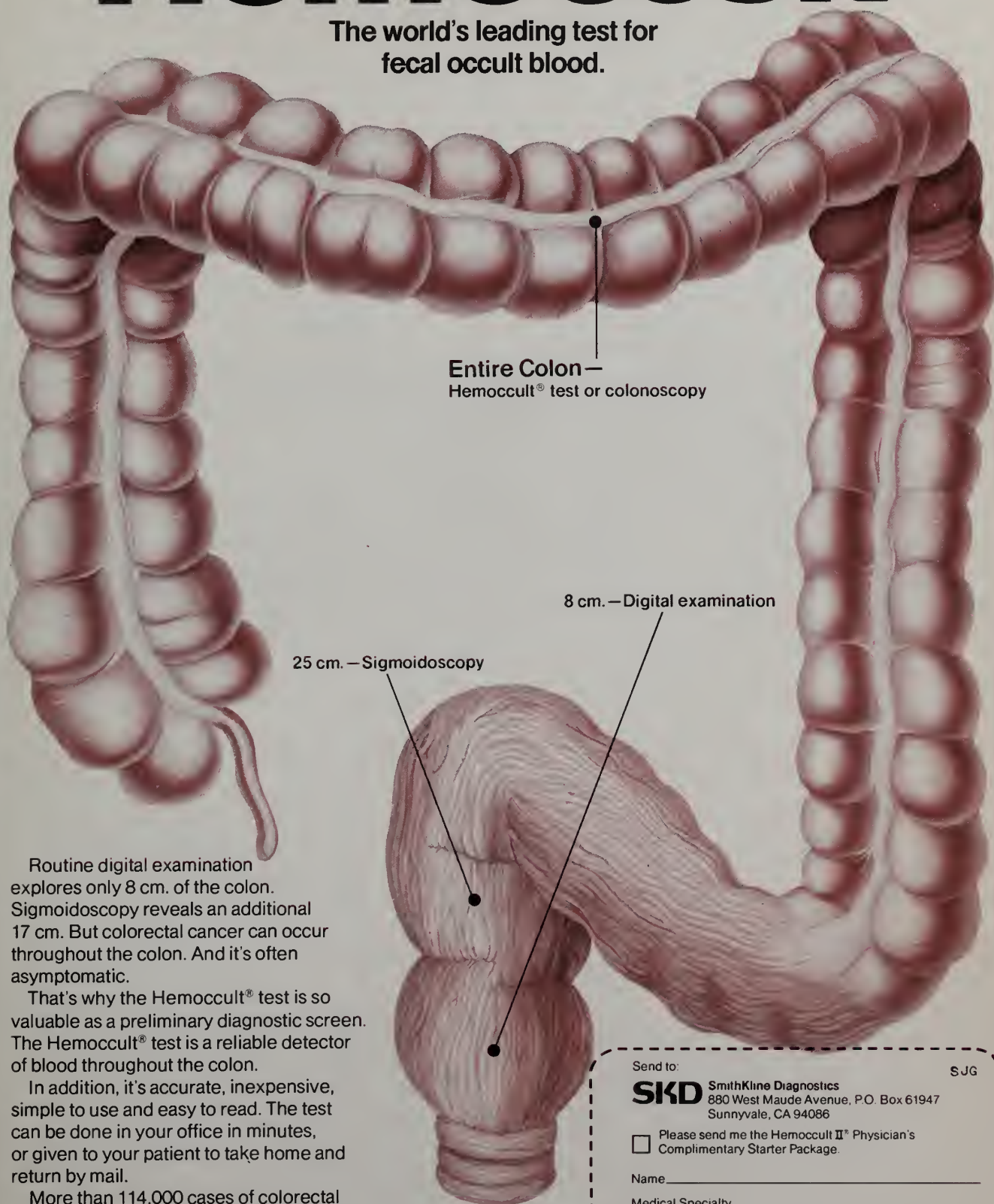
El Programa Determinación de Incapacidad del Seguro Social solicita neurólogos para examinar reclamantes y someter informe escrito. Para más información favor llamar: David Ramírez Santoni, MD - Teléfonos: 754-8910, 754-8915

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the Bowels



Constipation



Chronic
Constipation



Habituation to
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Perdiem™

Prescribing Information

ACTIONS: Perdiem™, with its gentle action, does not produce disagreeable side effects. The vegetable mucilages of Perdiem™ soften the stool and provide pain-free evacuation of the bowel. Perdiem™ is effective as an aid to elimination for the hemorrhoid or fissure patient prior to and following surgery.

COMPOSITION: Natural vegetable derivatives. A unique blend of psyllium and senna (Plantago Hydrocolloid with Cassia Pod Concentrate).

INDICATION: For relief of constipation.

PATIENT WARNING: Should not be used in the presence of undiagnosed abdominal pain. Frequent or prolonged use without the direction of a physician is not recommended. Such use may lead to laxative dependence.

DIRECTIONS FOR USE—ADULTS: Before breakfast and after the evening meal, one to two rounded teaspoonfuls of Perdiem™ granules should be placed in the mouth and swallowed with a full glass of warm or cold beverage. Perdiem™ granules should not be chewed. After Perdiem™ takes effect (usually after 24 hours, but possibly not before 36-48 hours), reduce the morning and evening doses to one rounded teaspoonful. Subsequent doses should be adjusted after adequate laxation is obtained.

IN OBSTINATE CASES: Perdiem™ may be taken more frequently, up to two rounded teaspoonfuls every six hours.

FOR PATIENTS HABITUATED TO STRONG PURGATIVES: Two rounded teaspoonfuls of Perdiem™ in the morning and evening may be required along with half the usual dose of the purgative being used. The purgative should be discontinued as soon as possible and the dosage of Perdiem™ granules reduced when and if bowel tone shows lessened laxative dependence.

FOR COLOSTOMY PATIENTS: To ensure formed stools, give one to two rounded teaspoonfuls of Perdiem™ in the evening with warm liquid.

DURING PREGNANCY: Give one to two rounded teaspoonfuls each evening.

FOR CLINICAL REGULATION: For patients confined to bed, for those of inactive habits, and in the presence of cardiovascular disease where straining must be avoided, one rounded teaspoonful of Perdiem™ taken once or twice daily will provide regular bowel habits. Take with a full glass of water or beverage.

FOR CHILDREN: From age 7—11 years, give one rounded teaspoonful one to two times daily. From age 12 and older, give adult dosage.

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HOW SUPPLIED: Granules: 100 gram (3.5 oz) and 250 gram (8.8 oz) canisters.



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Before prescribing, please consult complete product information, a summary of which follows:

Indications: Relief of anxiety and tension occurring alone or accompanying various disease states. Efficacy beyond four months not established by systematic clinical studies. Periodic reassessment of therapy recommended.

Contraindications: Patients with known hypersensitivity to the drug.

Warnings: Warn patients that mental and/or physical abilities required for tasks such as driving or operating machinery may be impaired, as may be mental alertness in children, and that concomitant use with alcohol or CNS depressants may have an additive effect. Though physical and psychological dependence have rarely been reported on recommended doses, use caution in administering to addiction-prone individuals or those who might increase dosage; withdrawal symptoms (including convulsions), following discontinuation of the drug and similar to those seen with barbiturates, have been reported.

Usage in Pregnancy: Use of minor tranquilizers during first trimester should almost always be avoided because of increased risk of congenital malformations as suggested in several studies. Consider possibility of pregnancy when instituting therapy; advise patients to discuss therapy if they intend to or do become pregnant.

Precautions: In the elderly and debilitated, and in children over six, limit to smallest effective dosage (initially 10 mg or less per day) to preclude ataxia or oversedation, increasing gradually as needed and tolerated. Not recommended in children under six. Though generally not recommended, if combination therapy with other psychotropics seems indicated, carefully consider individual pharmacologic effects, particularly in use of potentiating drugs such as MAO inhibitors and phenothiazines. Observe usual precautions in presence of impaired renal or hepatic function. Paradoxical reactions (e.g., excitement, stimulation and

acute rage) have been reported in psychiatric patients and hyperactive aggressive children. Employ usual precautions in treatment of anxiety states with evidence of impending depression; suicidal tendencies may be present and protective measures necessary. Variable effects on blood coagulation have been reported very rarely in patients receiving the drug and oral anticoagulants; causal relationship has not been established clinically.

Adverse Reactions: Drowsiness, ataxia and confusion may occur, especially in the elderly and debilitated. These are reversible in most instances by proper dosage adjustment, but are also occasionally observed at the lower dosage ranges. In a few instances syncope has been reported. Also encountered are isolated instances of skin eruptions, edema, minor menstrual irregularities, nausea and constipation, extrapyramidal symptoms, increased and decreased libido—all infrequent and generally controlled with dosage reduction; changes in EEG patterns (low-voltage fast activity) may appear during and after treatment; blood dyscrasias (including agranulocytosis), jaundice and hepatic dysfunction have been reported occasionally, making periodic blood counts and liver function tests advisable during protracted therapy.

Usual Daily Dosage: Individualize for maximum beneficial effects. Oral—Adults: Mild and moderate anxiety and tension, 5 or 10 mg t.i.d. or q.i.d.; severe states, 20 or 25 mg t.i.d. or q.i.d. Geriatric patients: 5 mg b.i.d. to q.i.d. (See Precautions.)

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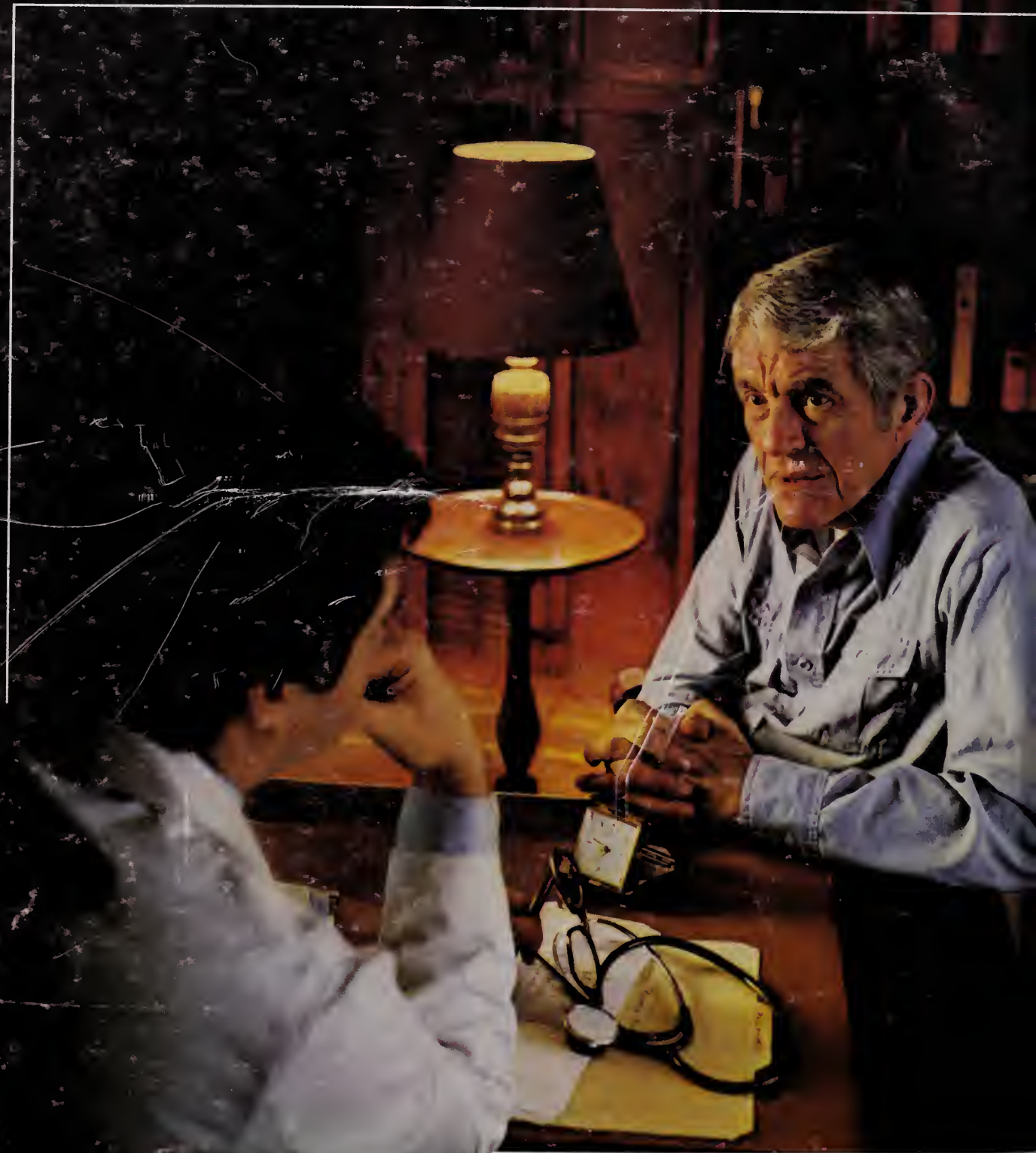
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Please see following page.

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Please see preceding page for a summary of product information



